

# ANNALS OF INTERNAL MEDICINE

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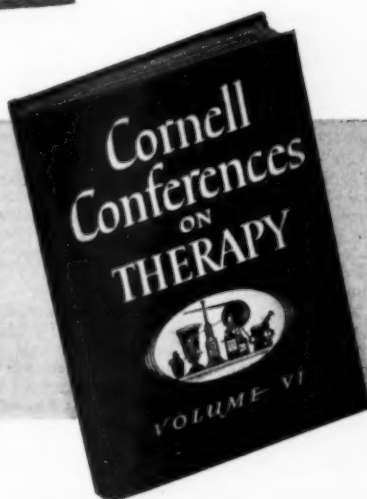
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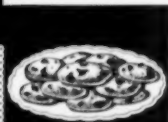
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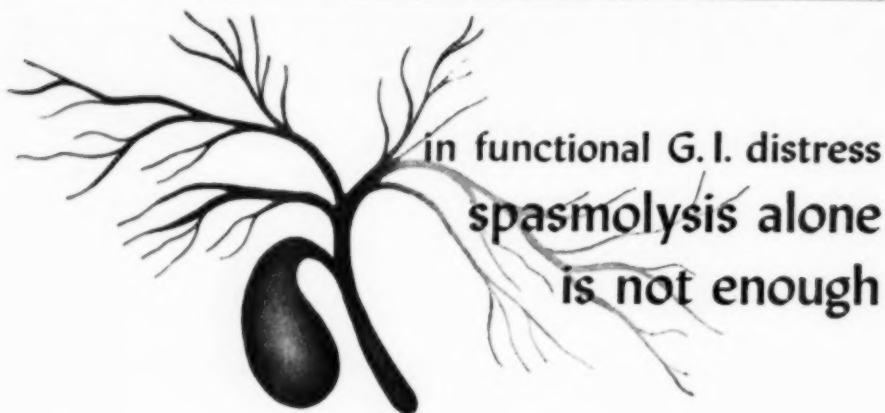
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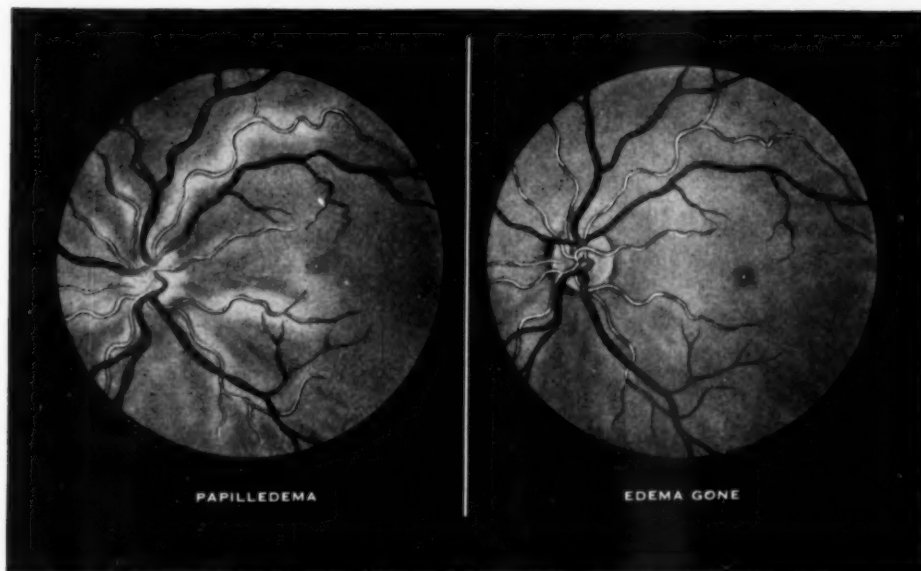
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2. Paton, W. D. M., and Zaimis, E. J.: Pharm. Reviews 4:219 (Sept.) 1952.

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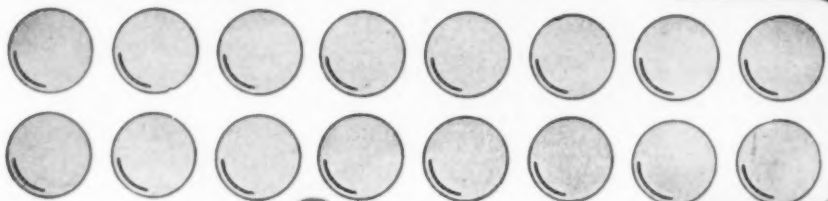
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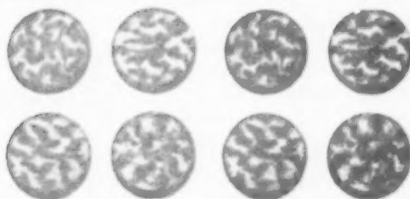
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2. Geddes, W.F.: Cereal Chemists Guard Nutrition, *Agricultural and Food Chemistry* 1:38 (Apr.) 1953.
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Crespo, S., and Bradley, W.B.: Calcium and Milk Content of Commercial White Bread. Report by the Laboratories of the American Institute of Baking, Feb. 28, 1950.



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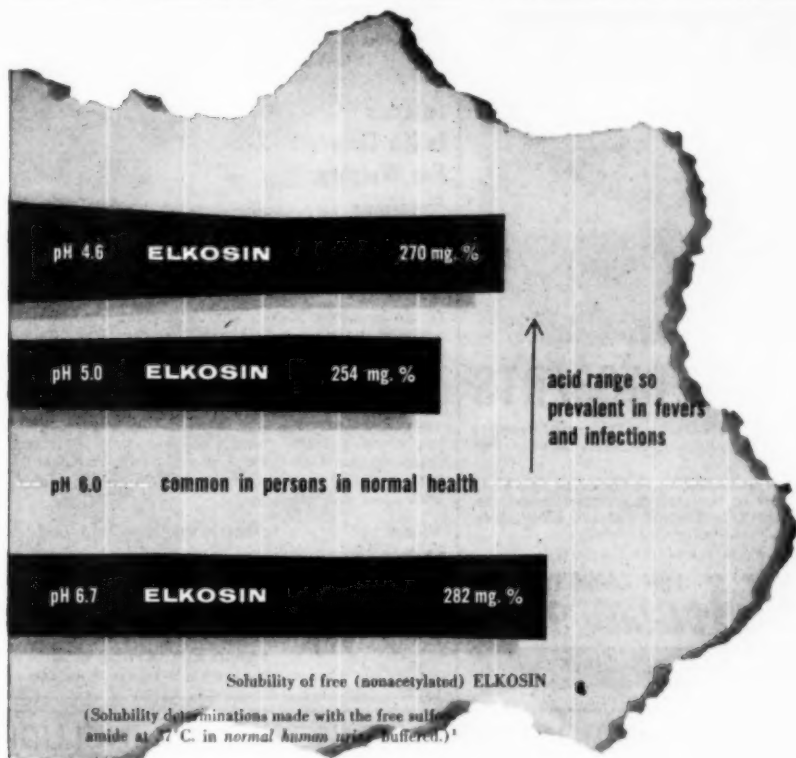
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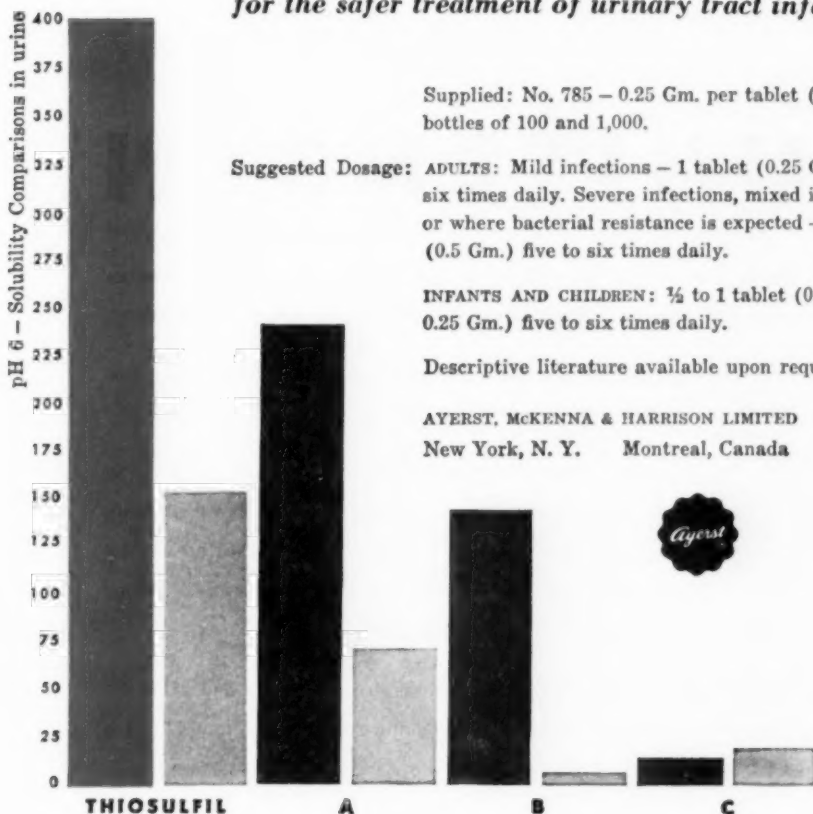
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The striking clinical benefits of BUTAZOLIDIN in arthritis and allied disorders cannot be due solely to analgesic effect since it has only moderate analgesic effect in non-rheumatic disorders.

an effective and potent anti-arthritic

BUTAZOLIDIN produces both improvement of function and relief of pain. In rheumatoid arthritis a recent report<sup>1</sup> indicates "major improvement" in 40 of 68 cases. Another notes "marked decrease in swelling, increase in range of motion, and increase in strength" in 41 per cent of patients with lesser improvement in an additional nine per cent.<sup>2</sup> A third study<sup>3</sup> records "appreciable pain relief" in 69 per cent of patients with 50 per cent showing objective evidence of improvement. Similar favorable results have been recorded in gout, spondylitis, osteoarthritis, bursitis, and other painful musculoskeletal disorders. These findings illustrate that BUTAZOLIDIN when properly used provides gratifying therapeutic benefit in a wide variety of painful and disabling disorders.

(1) Kunell, W. C., and Schaferick, R. W.; California Med. 77:319, 1952. (2) Stephens, C. A. L., Jr., and others; J.A.M.A. 150:1004 (Nov. 15) 1952. (3) Steinbrocker, O., and others; J.A.M.A. 150:1007 (Nov. 15) 1952.



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## DIBENZYLINE\*

for

PERIPHERAL VASCULAR DISORDERS

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HYPERTENSION OF PHEOCHROMOCYTOMA

'Dibenzyliline' is a potent, long-acting adrenergic blocking agent which can produce and maintain "chemical sympathectomy" by oral administration.

In *vasospastic conditions*, clinical investigators have found 'Dibenzyliline' to be extremely effective.

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*Available:* 10 mg. capsules in bottles of 100.

Note: Before administering 'Dibenzyliline', it is important that the physician be thoroughly familiar with the mode of action of the drug and recommended technique of administration. Full information is contained in S.K.F. literature, available on request.

\*T.M. Reg. U.S. Pat. Off. for phenoxybenzamine hydrochloride, S.K.F.

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*"most active  
in chronic,  
drug refractive  
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**Fumidil**

TRADE MARK

(Fumagillin, Abbott)

*a potent, new  
direct-acting  
antibiotic*

## FUMIDIL is specific for amebiasis

FUMIDIL acts directly against *E. histolytica*—both in the trophozoite and cyst forms—*yet doesn't disturb the normal flora in the intestinal tract.*

Thus, you can use it both to clear the carrier state and to treat the active disease.

## FUMIDIL is usually well tolerated

While mild side effects may occur at all dosage levels, they appear to be less frequent at lower dosages.

Reported side effects have not been of a serious character and have rarely necessitated withdrawal of medication.

## FUMIDIL is effective orally

Dose for the average adult is 30 to 60 mg. daily, divided over three or four times a day, for 10 to 14 days. You'll find one course of treatment with FUMIDIL clears most cases—and with surprisingly few recurrences. In simple-to-swallow 10-mg. capsules, bottles of 30. **Abbott**

1. Anderson, H. H., et al., Fumagillin in Amebiasis, Amer. J. Trop. Med. & Hyg., 1:552, July, 1952.

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Calories	3500
Protein	210 Gm.
Fat	30 Gm.
Carbohydrate	600 Gm.
Vitamins and Minerals	
Vitamin A	5000 units
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Ascorbic acid	300 mg.
Thiamine hydrochloride	10 mg.
Riboflavin	10 mg.
Niacinamide	100 mg.
Calcium parathenate	40 mg.
Pyridoxine hydrochloride	5 mg.
Choline bitartrate	500 mg.
Folic acid	2.5 mg.
Vitamin B <sub>12</sub> (crystalline)	4 mcg.
Iron	15 mg.
Calcium	6.3 Gm.
Phosphorus	4.5 Gm.
Sodium	1.9 Gm.
Potassium	7 Gm.

Sustagen contains powdered whole milk, non-fat milk solids, calcium caseinate and Dextrin Maltose plus vitamins and iron.

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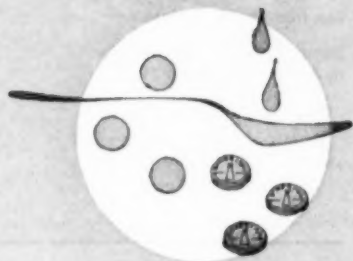
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# TRUE HEMATOPOIETIC STIMULANT IN ANEMIA THERAPY

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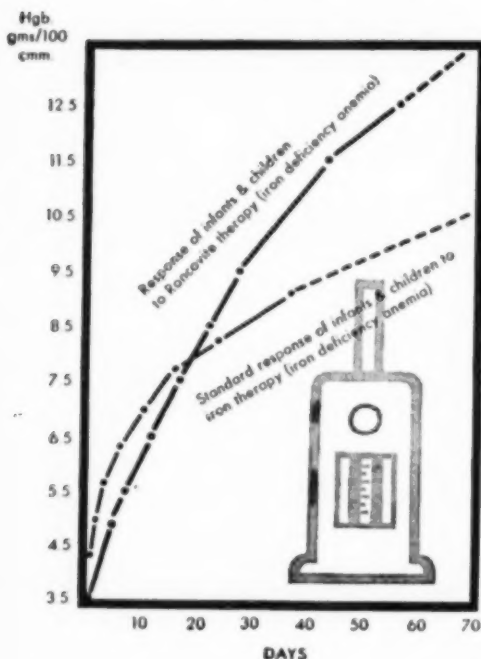
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In iron deficiency anemia where iron has been the standard treatment, Roncovite produces a faster response, greatly superior erythropoiesis and up to fourfold increases in the utilization of iron.<sup>1,2</sup>

In the anemia accompanying infection or chronic inflammatory disease, where iron is useless, Roncovite provides—in many cases—a striking and dramatic hematopoietic response.<sup>3,4,5,6,7</sup>

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Standard response chart, Josephs,  
H.J. J. Pediat. 49:246 (1931).

# RONCOVITE\*

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**Tablets**—each enteric coated, red tablet contains:

Cobalt chloride (Cobalt as Co...3.7 mg.).....15 mg.  
 Ferrous sulfate, exsiccated (Iron as Fe...60 mg.) .....0.2 Gm.  
 Average adult dosage—1 tablet after each meal and at bedtime.

*Supplied in bottles of 100 tablets.*

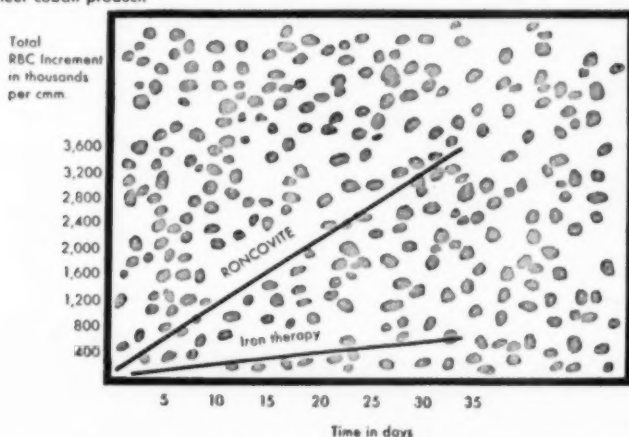
**Drops**—each 0.6 cc. contains:

Cobalt chloride (Cobalt...9.9 mg.).....40 mg.  
 Ferrous sulfate (Iron...15.1 mg.).....75 mg.  
 Average dose—0.6 cc. (10 minims) diluted with water, milk, fruit or vegetable juice once daily to infants and children.

*Supplied in bottles of 15 cc. with calibrated dropper.*

1. Wolff, H., Med. Monatsschr. 5:239 (1951); (2) Rohn, R.J., and Bond, W.H.: to be published; (3) Berk, W., et al: New England J.M. 240:754 (May) 1949; (4) Robinson, J.C., et al: New England J.M. 240:749 (May) 1949; (5) Weissbecker, W., and Maurer, R.: Klin. Woch. 24:855 (1947); (6) Wolff, H., and Barthel, S.: Munch. M. Wschr. 93:467 (1951); (7) Gardner, F.H.: J. Lab. & Clin. M. 41:56 (Jan.) 1953.

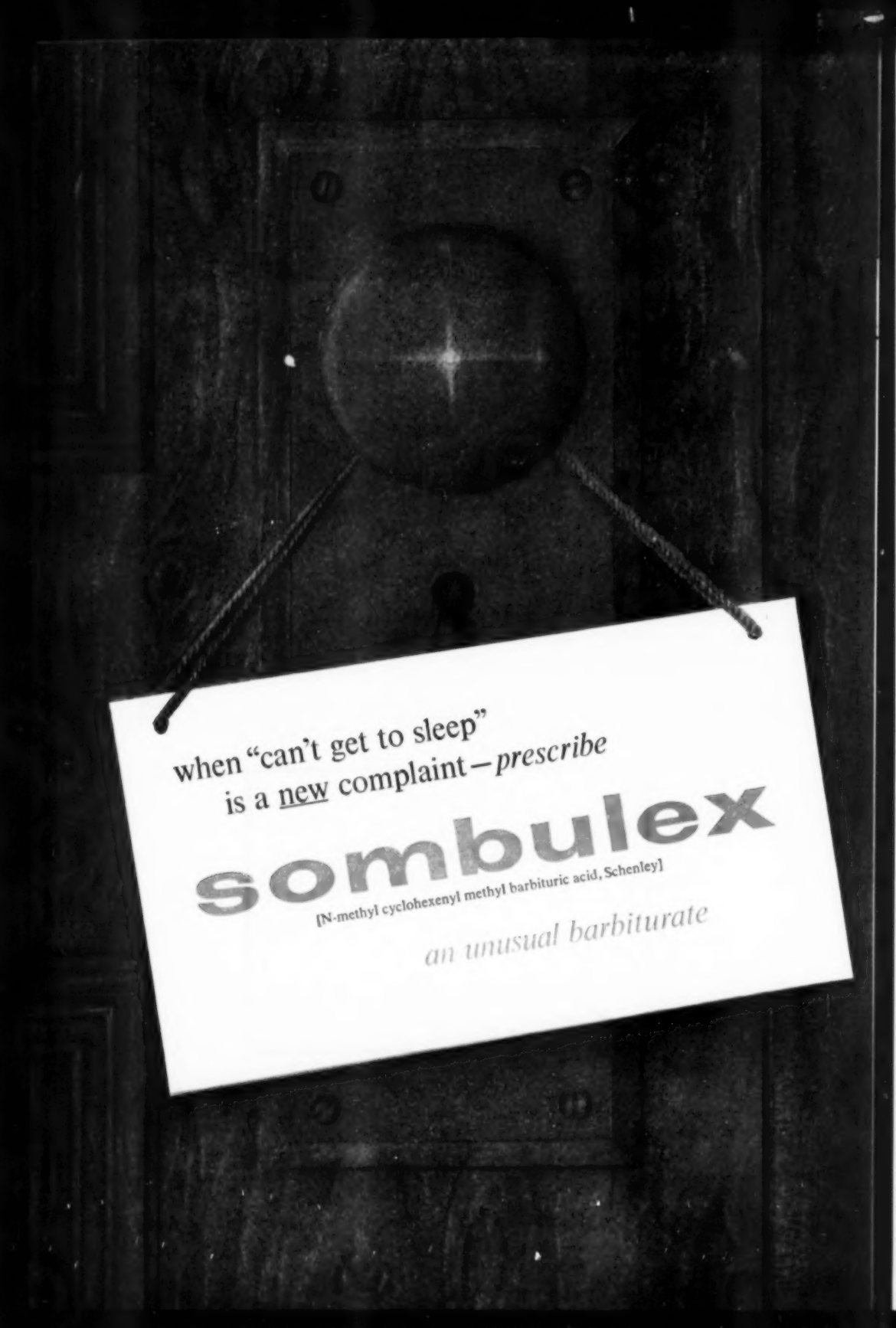
\*The pioneer cobalt product.



Comparison of the average erythrocyte response of iron-deficiency anemic children to Roncovite<sup>2</sup> and to iron therapy.—Computation—Method of Schiodt: Am. J. Med. Sci. 193:313 (1937).

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when "can't get to sleep"  
is a new complaint — *prescribe*

**sombulex**

[N-methyl cyclohexenyl methyl barbituric acid, Schenley]

*an unusual barbiturate*

## **sombulex\*** *is an unusual barbiturate*

because it works within 15 to 30 minutes and leaves the bloodstream within 3 to 4 hours, thus avoiding the danger of hangover for patients who do not need heavy barbiturate action.



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...when the mind won't let the body rest, and patients complain for the first time... "Doctor, I can't get to sleep"... SOMBULEX is the prescription of choice for these first-time barbiturate patients. For them, 1 or 2 tablets taken with water or a warm beverage usually suffice to induce a night's refreshing sleep without hangover. Patients will not readily identify SOMBULEX as a barbiturate.

### *The unusual uses of* **sombulex**

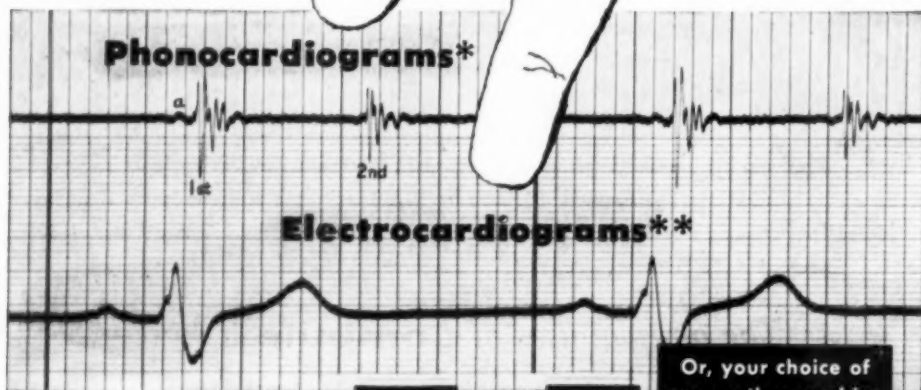
Because of its rapid yet nonpersistent action, 1 SOMBULEX Tablet will help restore *interrupted* sleep without subsequent hangover, or permit a relaxing cat nap before a busy evening. One SOMBULEX Tablet also will help the new night-shift worker adjust to a daytime sleeping schedule. NOTE: The action of SOMBULEX may be too short lived for the patient already dependent upon long-acting barbiturates. SOMBULEX is supplied in bottles of 100 tablets, each containing 0.26 Gm. (4 gr.) N-methyl cyclohexenyl methyl barbituric acid, Schenley.

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PHOTOGRAPHICALLY  
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are fully detailed recordings of ALL of the heart sounds and murmurs present. The location, pitch, duration, and intensity of a murmur are reproduced with the same completeness of detail as are the auricular, first and second sounds of the normal record shown above.

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1 to escape  
pollens



## 2 alternatives for the hay fever patient

2 to relieve  
symptoms



### **Pyribenzamine®**

hydrochloride  
(triphenylamine hydrochloride Ciba)

Once atop Pike's Peak, your hay fever patient can enjoy freedom from pollens. But for patients who must remain in a high-pollen environment, you can institute this effective therapy: one or two Pyribenzamine tablets, 3 or 4 times daily.

Alone and as an adjunct to desensitization, Pyribenzamine has proved effective in relieving hay fever symptoms, as evidenced by thousands of published case reports. On the basis of this evidence, no other antihistamine combines greater clinical benefit with greater freedom from side effects.

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### *not necessarily...*

Tedral, taken at first sign of attack, often forestalls severe symptoms.

*in 15 minutes...* Tedral brings symptomatic relief with a definite increase in vital capacity. Breathing becomes easier as Tedral relaxes smooth muscle, reduces tissue edema, provides mild sedation.

*for 4 full hours...* Tedral maintains more normal respiration for a sustained period—not just a momentary pause in the attack.

*Prompt and prolonged relief* with Tedral can be initiated any time, day or night, whenever needed, without fear of incapacitating side effects.

#### *Tedral provides:*

theophylline .....	2 gr.
ephedrine .....	$\frac{3}{8}$ gr.
phenobarbital .....	$\frac{1}{8}$ gr.

*in boxes of 24, 120 and 1000 tablets*

# Tedral

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*Laboratories* NEW YORK

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## ... for the obese patient ?

*Because*

Obedrin offers a practicable solution to the problem of keeping an obese patient on a restricted diet.

*Because*

Thousands of enthusiastic physicians have found that Obedrin curbs the appetite without making the patient jittery and does not cause insomnia.

*Because*

Obedrin contains enough vitamins to supplement the restricted diet. A large dose of vitamin C is included to help mobilize tissue fluids.

*Because*

Obedrin contains *Pentobarbital*, a short-acting barbiturate, as a corrective. *Pentobarbital* has approximately the same duration of action as methamphetamine, so the possibility of cumulative barbiturate effect is negligible.

**Available: The 60-10-70 Diet.\*** This is a convenient, variable diet, with enough roughage to eliminate necessity of artificial bulk laxatives.

Write for Data of daily Menus of the  
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Each Obedrin tablet contains:

Semoxidine HCl (Methamphetamine HCl)	5 mg.
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There are many reports  
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'Aerosporin' has brought  
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## *Polymyxin B Sulfate*



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'AEROSPORIN' Sterile, 500,000 Units, equivalent  
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### Bibliography:

1. Frank, P.F., Wilcox, C., and Finland, M.: In Vitro Sensitivity of Coliform Bacilli to Seven Antibiotics, *J. Lab. & Clin. Med.* 33:188 and 205, 1950.
2. Jawetz, E., and Coleman, V.R.: Laboratory and Clinical Observations on Aerosporin (Polymyxin B), *J. Lab. & Clin. Med.* 34:751, 1949.
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6. Jawetz, E.: Infections with *Pseudomonas aeruginosa* Treated with Polymyxin B, *Arch. Int. Med.* 59:90, 1952.



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**cortisone  
for inflammation,  
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Each gram contains:

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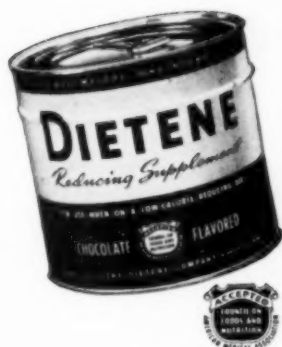
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Delicious-tasting Dietene Milk Shake (skimmed milk and Dietene) provides maximal amounts of protein, vitamins and minerals with a minimum of calories. Taken in mid-morning and mid-afternoon, it satisfies the appetite for food and makes it easier for the patient to adhere to his diet.

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No calorie-counting is required; no special preparations needed—the sheets are prepared without advertising, to look as though typed especially for the patient.

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**full**  
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**dosage**  
**of aminophylline**  
**ORALLY**

**Cardalin** tablets

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**Cardalin-Phen** tablets

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*with safety and simplicity*

*for the cardiac patient*  
*for the asthmatic patient*  
*for diuresis*

**Cardalin**  
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 tablets

Each tablet contains:

Aminophylline . . . . . 5.0 gr.  
 Aluminum Hydroxide . . . . . 2.5 gr.  
 Ethyl Aminobenzoate . . . . . 0.5 gr.

Cardalin-Phen contains, in addition, ¼ gr. of phenobarbital for sedation.

Cardalin and Cardalin-Phen tablets are best tolerated after meals and preferably administered with one-half glassful of milk.

Supplied: Bottles of 100, 500, 1000.

Cardalin and Cardalin-Phen contain 5 grains of Aminophylline per tablet... the highest concentration supplied for Oral Administration. Two protective factors (Aluminum Hydroxide and Ethyl Aminobenzoate) counteract the local gastric irritation so common to oral aminophylline therapy. Prolonged treatment at high dosage levels can be accomplished with Cardalin and Cardalin-Phen, as demonstrated by extensive clinical studies.

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In the form of AMINODROX, three out of four patients can be given therapeutically effective *oral* doses of aminophylline.

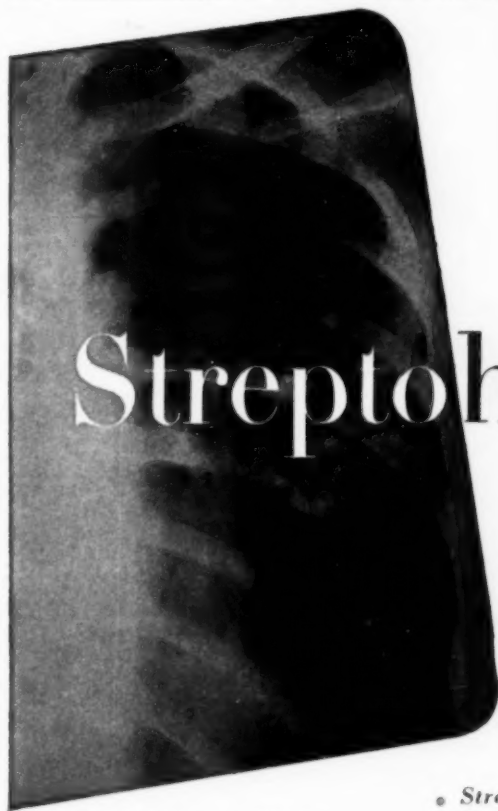
This is possible with AMINODROX because gastric disturbance is avoided.

Now congestive heart failure, bronchial and cardiac asthma, status asthmaticus and paroxysmal dyspnea can be treated successfully with *oral* aminophylline in the form of AMINODROX.

Aminodrox Tablets contain 1 1/2 gr. aminophylline with 2 gr. activated aluminum hydroxide.

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Also available with 1/4 gr. phenobarbital.



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NOW...

a new, powerful,  
antituberculosis  
combination

a new crystalline compound  
of the two preferred  
antimicrobials for  
treatment of tuberculosis

<sup>\*</sup>Brand of Streptomycylidene  
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- Streptomycin produces minimal incidence of hearing loss over extended treatment periods.
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... and for streptomycin-resistant tuberculosis—

new Viocin (brand of viomycin): In vials containing 1 Gm. crystalline viomycin sulfate in sterile, dry powder form.



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# what more could a supplement provide?

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How Ovaltine in milk approaches this concept, and how well the recommended three glassfuls daily augment the nutritional intake, is shown in the appended table. The two forms of Ovaltine available—plain and chocolate flavored—are closely alike in their nutrient values.

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(Each serving made of  $\frac{1}{2}$  oz. of Ovaltine and 8 fl. oz. of whole milk)

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CHLORINE.....	900 mg.	BIOTIN.....	0.03 mg.
COBALT.....	0.006 mg.	CHOLINE.....	200 mg.
*COPPER.....	0.7 mg.	FOLIC ACID.....	0.05 mg.
FLUORINE.....	3.0 mg.	*NIACIN.....	6.7 mg.
*IODINE.....	0.15 mg.	PANTOTHENIC ACID.....	3.0 mg.
*IRON.....	12 mg.	PYRIDOXINE.....	0.6 mg.
MAGNESIUM.....	120 mg.	*RIBOFLAVIN.....	2.0 mg.
MANGANESE.....	0.4 mg.	*THIAMINE.....	1.2 mg.
*PHOSPHORUS.....	940 mg.	*VITAMIN A.....	3200 I.U.
POTASSIUM.....	1300 mg.	VITAMIN B <sub>12</sub> .....	0.005 mg.
SODIUM.....	560 mg.	*VITAMIN D.....	420 I.U.
ZINC.....	2.6 mg.		
*PROTEIN (biologically complete).....		32 Gm.	
*CARBOHYDRATE.....		65 Gm.	
*LIPIDS.....		30 Gm.	

\*Nutrients for which daily dietary allowances are recommended by the National Research Council.

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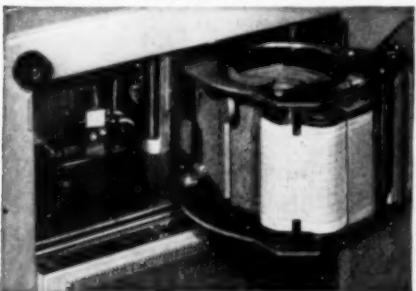
## offers 5 big advantages



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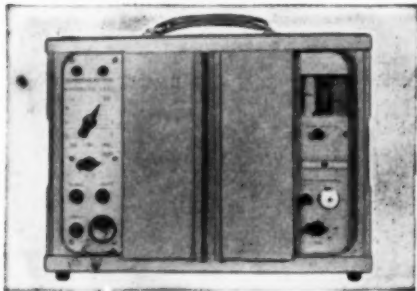
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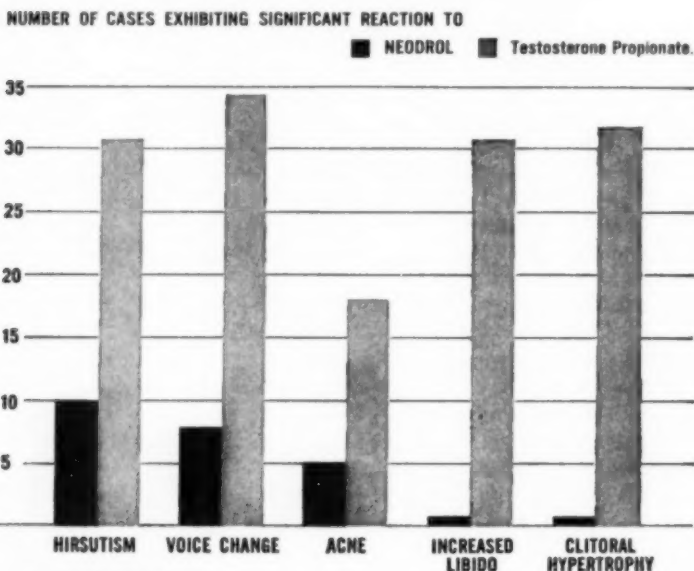
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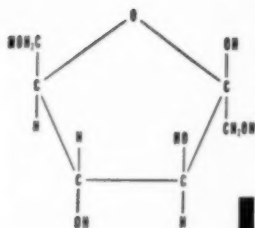
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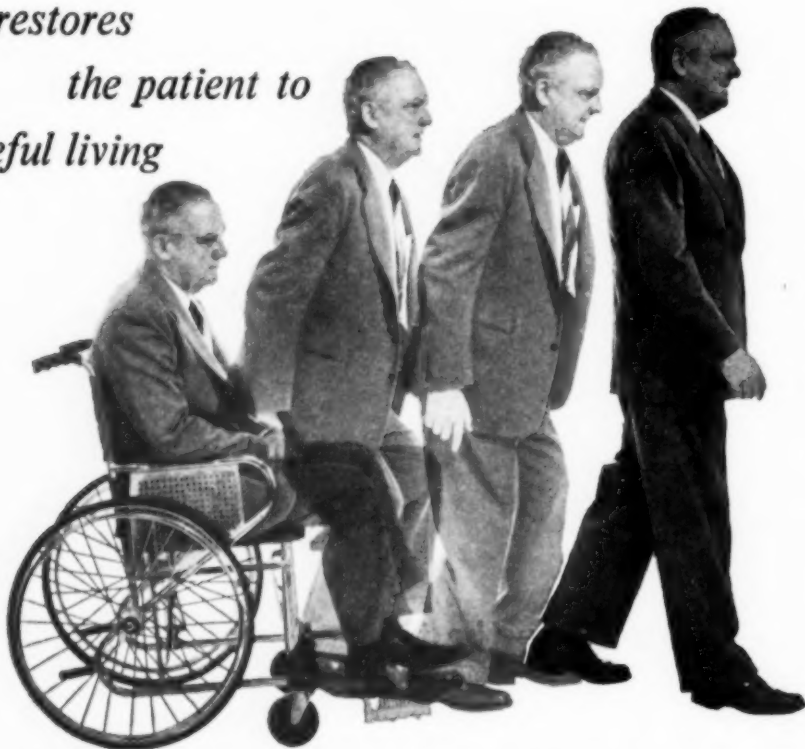
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# ANNALS OF INTERNAL MEDICINE

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## THE RESPONSIBILITIES OF THE FELLOWS OF THE AMERICAN COLLEGE OF PHYSICIANS \*

By T. GRIER MILLER, F.A.C.P., *Philadelphia, Pennsylvania*

At this time I have the obligation, as well as the pleasure, of addressing you on some subject that I believe to be of interest to our College. My remarks will be addressed primarily to its younger members, especially to those of you who are being admitted to Fellowship at this Convocation. The future of our organization is in your hands. Soon you will be its officers, its regents and its governors. Each of you is a potential factor in its progress. Although, as physicians, all of you are members of other medical organizations, none of them presents to you, as internists, certain opportunities afforded by this College. Corresponding responsibilities are involved.

To appreciate the position of your College in American medicine, you must know its traditions, its accomplishments and its current aims. To maintain and to advance its service to the profession and the public, you must have the imagination, the initiative, the patient zeal and the unselfish spirit that characterized its founders and their immediate followers. This knowledge and these personal attributes are essential to your success in meeting adequately the responsibilities that now devolve upon you as Fellows.

In spite of the tribulations of the College in its first decade, as related in a previous presidential address (Martin, 1929), the determination and the persistence of its early sponsors led, in 1926, to the realization of their dream of a truly great organization of internists. At that time Alfred Stengel, although not one of its founders, became its president. Largely as a result of his wisdom and tireless efforts, together with those of Charles F. Martin, of Montreal, a subsequent president, a complete reorganization took place. After this was accomplished many prominent and similarly gifted practitioners and teachers of medicine throughout the United States

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\* Convocation Address, Thirty-fourth Annual Session, American College of Physicians, Atlantic City, New Jersey, April 15, 1953.

and Canada were brought into its councils. Since then, due in the main to the indefatigable efforts of the members of its governing bodies and of its executive secretary, loyally supported by its Fellows, steadily increasing and noteworthy progress has been made.

During the 38 years of its existence the stated objectives of our College have been: Improvement in the educational status of its members and their colleagues, perpetuation of the best traditions of medicine, and maintenance of the dignity of the profession in relation to public welfare. Its Annual Sessions, as well as other activities, have been planned on such a basis. As early as 1922 publication of a journal was begun; originally the *Annals of Clinical Medicine*, the title was changed to *Annals of Internal Medicine* in 1927. First under the editorship of Aldred Scott Warthin and, for the past 20 years, of Maurice C. Pincoffs, the journal has had an outstanding influence on the maintenance of the objectives of the College. In 1934, during the presidency of George Morris Piersol, research fellowships for the further training of exceptionally qualified young physicians were established. In 1935, during President Meakins' administration, plans were laid for the subsequent establishment of the American Board of Internal Medicine. This came about as a result of insistence by Dr. Piersol, then Chairman of the Credentials Committee, that some educational yardstick be devised for admission to Fellowship. In 1936 President Bradley put our Regional Meetings on a sound foundation. They now have an annual total attendance of over 3,000. In the following year, as a result of the efforts of Edward Bortz, then a Governor, our Postgraduate Courses were developed. They now have an annual attendance of about 1,200. In 1939, in a further effort to improve the educational status of internists, President O. H. Perry Pepper brought about the first close coöperation of our College with another national medical organization, the American Medical Association, by the establishment of the Conference Committee on Graduate Training in Medicine. Now, due largely to the influence of our incoming President, LeRoy H. Sloan, we are coöperating with the American College of Surgeons, the American Hospital Association, the American Medical Association and the Canadian Medical Association in a Joint Commission on the Accreditation of Hospitals. In 1949 Cyrus C. Sturgis, presently nominee for President-Elect, secured the financial support of the Kellogg Foundation for the selection, placement and special training in this country of promising South American internists. Finally, in 1950, one of our most loyal Regents, A. B. Brower, who will receive the Stengel Award this evening, generously established a trust fund to provide, for one month of each year, a Traveling Scholarship. Because of the uniqueness and popularity of this scholarship, we have now added a second similar one. We also have unofficial representation on the Division of Medicine of the National Research Council, the United States Pharmacopoeial Convention and the Gorgas Foundation.

In support of its interest in medical research, the College recognizes distinguished accomplishments in the clinical sciences and in preventive

medicine by the bestowal annually at these Convocations of the John Phillips and the James D. Bruce Awards. These were established in 1929 and 1946, respectively.

In addition to its educational objectives, the College has put much emphasis on the personal qualifications of its members. Professional ability alone does not qualify for Fellowship. One must also possess an irreproachable character, a humanistic attitude and a genuine concern about his own continued development and about the progress of medicine. These personal attributes are essential for the application of the art and science of medicine to the benefit of colleagues and patients. Although such qualifications are required for admission to Fellowship, the College attempts further to develop them in its members by stimulating personal contacts at its various meetings and by the bestowal each year of the Alfred Stengel Award. It was primarily for the recognition of such qualifications, including loyalty and service to the College, in some one of its officers, Regents or Governors, that James D. Bruce, a former president, bequeathed a fund for the establishment of this award.

Such a background of tradition, of accomplishment and of ideals is gratifying. We must not relax our continued efforts to promote the welfare of our College, the medical profession and the public. As our predecessors visualized opportunities for progress and converted them into realities, so must we today. To stand still is to retrogress. What, specifically, are our present responsibilities? In outlining some of them, I trust that you will appreciate that they represent the thought of a single Fellow, presented with the hope of stimulating in each of you further interest in the subject.

*First* on my list of our responsibilities is the selection of new members. Already I have indicated the established principles. Since professional competence is a requisite, certification by the American Board of Internal Medicine is the most objective criterion. In my opinion it should continue to be required in all but the most exceptional instances. It is especially demanded in the evaluation of candidates from nonteaching and nonresearch centers. In this way only, in many instances, can we adequately appraise professional qualifications. I believe, however, that under special circumstances we should continue to admit directly to Fellowship certain able internists, as well as distinguished scientists, even though they are not certified by the Board. Such men not infrequently have risen to important clinical positions, including the chairmanship of departments of medicine. Some, who have come up by way of the fundamental medical sciences, have spent long years in special research projects, at times under fellowships that precluded training in the broad field of medicine. Consequently they have never had the time or opportunity to prepare for the examinations of the Board. Such men should not be denied Fellowship merely because of their failure to be certified.

It has been determined that, in 1952, 56.5 per cent of those with the rank of Associate or higher on the teaching staffs of the medical schools of the United States and Canada were Fellows or Associates of the College. Some of the other 43.5 per cent are now in the process of being admitted. Others, though certified, have not otherwise met our standards for admission. This leaves only 10 to 15 per cent who are fully qualified. Some of these have not yet appreciated the advantages of membership in the College. Many of them, however, would welcome the opportunity to join the College and take part in its activities. They now should be proposed.

The initiation of all proposals for membership is the prerogative of the individual Fellows of the College. In order to meet this responsibility, you should survey the young internists with whom you are intimately acquainted and place in nomination those who, in your judgment, meet the accepted requirements. Furthermore, you should not hesitate to be equally critical in your evaluation of those proposed by others. You should stand ready to make appropriate comments, favorable or otherwise, about such candidates. In judging them, you should give due consideration not only to their professional but also to their personal qualifications. In the latter respect especially you must assume responsibility. Our Committee on Credentials is largely dependent on the local Governor and his Fellows for advice as to character, ability to get along satisfactorily with colleagues and patients, interest in the human side of medicine and capacity to keep abreast of, and to advance, the art and science of medicine.

A *second* responsibility to the College is support of its established activities. These include its various meetings and also certain organizational functions necessary for smooth operation and for the maintenance and advancement of its influence in the broad field of medicine. The meetings of the College are designed primarily for the educational and social uplift of its Fellows and Associates, but nonmembers are welcomed to its Regional and Postgraduate meetings, and the deliberations at its General Sessions are available to the profession through publication in the *Annals*. As Fellows, therefore, you have not only the obligation of attending its meetings, for personal educational and inspirational purposes, but also the opportunity, by means of them, to present to your fellow members and to the entire profession such significant contributions as you are able to make. At this Annual Session 500 or more members are taking some part in its proceedings. Many others do so in the Regional Meetings and Postgraduate Courses. Although not all of you can assume such a responsibility to the College, every one can attend the meetings and so prepare himself the better for his daily activities in practice. Furthermore, as Fellows, you have an obligation to attend the Annual Business Meeting and the Convocation of the College, as well as the banquet and other social functions, in order fully to appreciate the background, the set-up and the objectives of the organization.

Also, from time to time many of you will have obligations and responsibilities of an administrative, consultative and advisory nature thrust upon you. We have in Mr. Loveland a highly qualified, experienced and devoted executive officer, but he and his efficient staff cannot carry the entire administrative burden. Neither can the officers, the Regents and the Governors meet all the demands made upon them. Fellows from the membership at large must be chosen for committee activities, for representation of the College on various Boards and at special meetings of other organizations, and for advice regarding special technical and professional matters. In this regard I am glad to state that, to my knowledge, rarely has any Fellow hesitated to accept the responsibility for any office, any committee membership or any personal activity properly assigned to him. It is only by such cooperation that the College is able to meet its obligations for meetings, for deliberations regarding policies and for the accomplishment of its other organizational functions.

A *third* responsibility of a Fellow is to become, within the range of his ability, the best possible personal representative of his field of medical endeavor. This may be as a practitioner, a teacher or an investigator. For those of you who are clinicians, who constitute the great majority of the membership, this implies many things: medical knowledge and the skill to apply it; an understanding of human nature and the capacity to utilize it in your relationships with patients and colleagues; personal integrity and the art of developing and maintaining friendships.

It is not enough to be familiar with the segment of medical knowledge that bears on your particular field of activity; you should also have at least some understanding of related fields and some appreciation of the history and background of medicine. You should keep abreast of and appraise the current medical literature. Furthermore, you should constantly be in the process of learning from your own experience by making detailed observations on your patients, meticulously recording and analyzing the accumulated data, and from time to time making such contributions as you can at meetings and in the literature. In so doing one acquires good judgment, the skill of applying his talents to the benefit of patients and the technic of imparting his knowledge to others.

To utilize one's accomplishments to a maximal extent one also must have a broad understanding of human nature. This may be cultivated by stimulating contacts with others in the home and community, at meetings such as ours, in the course of travel, and by the conscious study of the reactions of people under varying conditions. Thus one learns to appreciate the emotional as well as the physical reactions of the patient. Those who adopt such a program meet a responsibility to the College, as well as to themselves and their patients, by becoming better physicians.

Above all, however, a Fellow's influence in the practice of medicine depends on his personal integrity, his fair dealing with colleagues, his

honesty and forthrightness and a selfless concern for the dignity of the profession. Although such personal attributes stem largely from one's heredity, family background, early training and environment, our College provides facilities for their encouragement: stimulating contacts with each other at its various business, scientific and social meetings. Only by such personal qualifications can the physician inspire his patients, secure their confidence, maintain their loyalty and make his greatest contribution to the welfare of his College.

In so meeting your personal responsibilities as a practitioner—and this applies equally to teachers and to investigators—you will be living up to the vows that you will take this evening in accepting the Fellowship Pledge of the College: to live in conformity with its ideals and regulations. This involves, even before your own welfare, that of your patients, cordial and honest relations with your colleagues and service to the public.

Thus my brief appeal to you, the younger Fellows, is to discharge your obligations to your College in such fashion as to preserve its traditions, to enhance its educational and other organizational activities, and to uphold the dignity of the profession. As a means to this end I have suggested particular care in the selection of new Fellows, participation in College activities, readiness to accept administrative, consultative and teaching responsibilities, and the leading of exemplary lives. The rewards for the assumption of such responsibilities include not only the satisfaction of having made a contribution to the welfare of the College, but also of having rendered a service to medicine and the public.

## PERIODIC HEALTH EXAMINATIONS \*

By FREDERICK H. SHILLITO, M.D., F.A.C.P., *New York, N. Y.*

### INTRODUCTION

INTEREST in periodic health examination programs is increasing. Larger and larger industrial groups are undergoing regular periodic health surveys. Individuals, stimulated by insurance companies and other enlightened agencies, are seeking out this phase of preventive medicine. Veterans of our military service, particularly from such groups as flying personnel of the Air Force, have been indoctrinated in the idea of frequent surveys of the physical status of the individual.

Irrespective of the ways and means of motivation, the individual turns to the medical profession for the accomplishment of the examination. The doctor is the corner-stone of the entire program. He is the one who must devote his time and energy to bring the plan to a successful end. It is a somewhat new phase of the practice of medicine, and is a task which must of necessity be crowded by the physician into what may already be an overloaded day. The work of physical examinations cannot be delegated by the physician to any other group. The potentialities of this rapidly growing phase of clinical medicine are rather startling. To examine thoroughly every man, woman and child in the United States at least once a year would take the full time of about half of our practicing physicians. Though no one expects such an avalanche, time and thought must nevertheless be given to routine physical examinations so that they can be carried out efficiently. It is necessary to appreciate what can and what cannot be accomplished. The internist, of all specialists, is by training and nature best qualified to carry out an extensive and thorough individual health survey. This group cannot do all of the examinations, but it should lead the field in understanding and accomplishing the most productive and successful examination programs. Already many internists are actively engaged in the work, especially in carrying out so-called "executive" examinations. Such work is done in the physician's own office or hospital, and every kind of laboratory aid is utilized. With so little restraint upon him, it is a challenge to the internist, to guide all this endeavor along lines productive of real results, i.e., increasing productive capacity and better health of the examinee.

The medical literature in regard to health examinations is not extensive. Surveys of large numbers of examinations have been reported in a few instances. Johnson<sup>1</sup> states that in series of examinations running as high as 1,000 only 18 per cent can be said to show no abnormality. I believe that every physician would be in substantial agreement with this finding. The

\* Presented at the Thirty-fourth Annual Session of the American College of Physicians, Atlantic City, New Jersey, April 14, 1953.

significance of some of the deviations from the normal, found in four out of five examinees, is questioned by some. Kuh<sup>2</sup> questions the importance of many of the so-called abnormalities. I believe it is fair to summarize these differences by noting that examinees seen for the first time will show definite deviations from so-called normality in 80 per cent of cases. Subsequent examinations (annual or periodic), however, usually show chiefly a reiteration of previously noted abnormalities. Recent tabulations<sup>3</sup> show that electrocardiographic abnormalities in the overweight are half again as frequent as those whose weight falls within the normal range.

#### RESULTS OF PERIODIC HEALTH EXAMINATIONS

Primarily, a program of periodic health examinations results in a generally higher level of sensible health practices in the group examined. The individuals become health-conscious as to being overweight, indulging in poor posture, neglecting proper corrective physical exercise, exhausting themselves nervously and emotionally by overstrain, overindulging in stimulants and tobacco, and following highly inadequate diets. A group of individuals given periodic physical examinations should be a healthier, happier and better adjusted aggregation than their confrères who ignore the whole idea of individual periodic health appraisals.

Any physician who has carried out routine periodic examinations will agree that such a program does not uncover a multitude of dramatic and diverse acute pathologic entities. The deviations from the norm which occur in four out of five examinees are such things as weight, blood pressure, vision, hearing, electrocardiographic changes, urinary abnormalities and the like. The first signs of pneumonia, cerebral hemorrhage, coronary thrombosis and gastrointestinal hemorrhage will be discovered only by coincidence at the calendar health examinations.

As our store of medical knowledge grows it will be possible, we hope, to advise behavior to our examinee which may prevent or postpone the health catastrophes which now are the lot of men. Forthcoming fundamental research will provide such aids to us. In spite of careful, thorough and thoughtful health examinations, we still must expect the occurrence of health disasters, often in the interim between the dates of scheduled periodic health examinations. A few cases will suffice to illustrate this point.

*Case 1.* This 33 year old male was first examined in February, 1942. The examination included extensive history, very thorough physical examination, and complete laboratory work, including urinalysis, blood count, sedimentation rate, serology, basal metabolism, electrocardiograph, x-ray of chest, etc. After the original examination he was examined regularly at yearly intervals. The periodic examinations roughly approximated the original examination. The last of the periodic examinations was in March, 1952. This examination included an x-ray of the chest which showed no deviation from the normal. It was noted that he was 30 pounds overweight but was otherwise in excellent general health. Approximately nine months later he developed pain in his chest and x-rays revealed a mass in the mediastinum.

Subsequently there was bronchoscopy, surgical exploration and biopsy. Microscopic study revealed lymphosarcoma. It is noteworthy that the x-rays taken nine months previously were carefully reviewed and showed no indication whatsoever of the tumor, which may have been in its incipient stage at that time.

*Case 2.* This 31 year old male was given his original health examination in April, 1952. A very complete history and physical examination were carried out. The genitals were examined and found to show no variation from normal. Laboratory investigation indicated urinalysis, blood count, sedimentation rate, x-ray of chest, electrocardiograph, audiogram, serology, etc., as normal. Approximately five months later swelling of the right testicle was noted; right orchiectomy and biopsy revealed seminoma of the right testis.

*Case 3.* This 37 year old male was first examined in 1944, with a complete history, physical examination and extensive laboratory studies. Examination included a careful neurologic survey. Subsequently he was examined completely and thoroughly at approximately yearly intervals, with revelation of no important physical abnormalities and no abnormal neurologic manifestations. His last regular examination was in January, 1950. Approximately 10 months later he suffered a mild convulsive seizure. A very extensive neurologic study included hospitalization, inter-arterial injection, etc., and revealed a large angioblastic formation in the anterior temporal and lower frontal region of the skull. Obviously this was a congenital lesion, but it had been symptomless. It never was apparent during any of the long series of very careful periodic health examinations.

Appreciation of experiences such as those illustrated by the cases cited should in no way discourage examiner or examinee as to the advisability of initiating a program of periodic health examinations. Although these cases do show that physical examinations are not an impenetrable barrier to the onset of certain disease states, it is not difficult to recite examples of correctable defects detected at routine examinations. The following cases demonstrate positive results uncovered by routine methods. These conditions are of significance clinically and were completely incipient.

*Case 4.* In this case the original examination was carried out in 1943. Slight x-ray changes in the pulmonary root shadows were detected. These were studied with great care. A chest specialist agreed that the shadows were of no clinical significance. The patient was allowed to work, and over the next five years reported regularly for his annual periodic physical examination. Particular attention was paid to the pulmonary areas, and the previously observed lesion remained quiescent. At his annual examination in January, 1949, however, the chest x-ray showed a change from previous film. There was evidence of activity in the right apex. A short course of specific therapy was sufficient to effect a satisfactory cure. He was able to return to full duties. This case is an example of active pulmonary pathology uncovered at a calendar periodic physical examination. There had been no symptoms whatever which would have influenced this individual to be examined. The condition was uncovered purely because of the routine of regular examinations. It was a fortunate discovery, as further delay in detection would have lengthened the period of treatment and convalescence.

*Case 5.* This 32 year old male was originally examined in April, 1944. Thereafter he was examined annually with numerous ancillary aids such as hematologic studies, electrocardiograms, audiograms and x-rays. During this time he was traveling extensively. No symptoms referable to the gastrointestinal tract appeared. His most recent periodic examination was in December, 1952. Again he was without

gastrointestinal symptoms at the time of his calendar check-up. A routine stool examination showed the presence of *Endamoeba histolytica*. With this information, secured routinely only because he had reported for his annual health appraisal, it was possible to institute specific therapy and probably to avoid the occurrence of chronic amebiasis, which would have supervened if the *Endamoeba histolytica* infestation had not been cleared.

Probably the most definite and valuable result of an examination program is the relationship established between the physician and examinee. As rapport develops, the individual is moved to report promptly to the physician whenever acute symptoms appear. At the time of examination the physician is a friendly adviser. The examinee is told not to hesitate to seek information at any time. Although most symptoms are the results of relatively minor illnesses, such as sinusitis, prostatitis, gastroenteritis and skin infections, they are also the harbingers of more serious conditions. The hope of cure of almost all disease is early diagnosis. Unless health consciousness is promoted in the individual, procrastination will occur. Symptoms will be explained away until they become so disabling that there is no choice but to go to a physician. If for no other reason, periodic health examination programs are justified because of the rapport established between the physician and examinee.

#### OBJECTIVES OF PERIODIC HEALTH EXAMINATIONS

When a physician is approached by an individual or a group of persons interested in periodic health examinations, a conference should be held with those making the arrangements. Before the actual work is started, a plan should be agreed upon by all concerned. Ill planned examinations will result only in an enormous expenditure of energy without demonstrable results. For a year or two the novelty of examinations, particularly if they include impressive laboratory and x-ray procedures, will be sufficient to hold interest. Eventually, however, unless definite objectives have been achieved, the program will be dropped.

Examinations varying widely in scope and elaborateness are being carried out in connection with health maintenance programs. Often they are colored very strongly by the special scientific interests of the physician. Of course it is appreciated that clinical physical examinations are not carried out in exactly the same way by any two physicians. Slightly different modes of approach and execution will always occur. The individualized procedures are advantageous, and it would be deplorable if examinations were stereotyped and those carried out by one physician were the exact image of those of another examiner. Examinations can be categorized, however, in regard to objectives to be achieved. Here is where complete understanding must be reached between the physician and his group of examinees. The method of carrying out the examination should by all means be the prerogative of the examiner. The following outline is presented as a basis of discussion

between all interested parties before actual examining is undertaken. Disappointment and even criticism can be avoided if everyone understands that results can be anticipated only to the extent of the means employed. Decision should be reached as to what objectives are to be attained. Thereafter, the appropriate individual examination routine can be outlined easily.

*First Objective:* To establish a friendly contact and rapport between examinee and physician.

This result is obtained by an unhurried, quiet consultation period between physician and employee. Stress is laid upon reporting symptoms so that adequate investigation can be carried out. In this interview, insight can be gained by the physician into the patient's mental and emotional state. Even superficial psychiatric appraisal is of greatest importance. To relieve a man of worry or emotional strain is to render one of the greatest possible services to him.

*Second Objective:* To discern the most easily recognized correctable deviations from the norm (such as weight, auditory and visual acuity, prostate, hernias, blood pressure, posture, cardiac and respiratory reserve, skin lesions, muscle tone, etc.)

Essentially, the physical examination is the means of discovering these defects. The procedure is very worth while, as at least four out of five examinees will show some correctable deviation from the normal state. This method, however, does not uncover deep-seated and masked disease in its early stages.

*Third Objective:* To detect chronic debilitating conditions (arthritis, renal insufficiency, blood dyscrasias, pulmonary and cardiac lesions, gastrointestinal abnormalities, diabetes, tuberculosis and thyroid disorders).

To uncover disorders in this category, the examining physician must have at his disposal such aids as clinical pathological laboratory, x-ray equipment, electrocardiograph, etc. The incidence of some of these conditions is so high that certain laboratory procedures are carried out routinely. Others are carried out as a follow-up of hints and suggestions uncovered by the history and physical examination. This procedure is comparable to the usual diagnostic study for a practicing physician.

*Fourth Objective:* To discover early and incipient disease processes.

The conditions referred to in this category are statistically few in any group. We are assuming that they are being sought for in a phase when they are completely symptomless. It is obvious, therefore, that they must be searched out by the dragnet or case-finding method. This means the general application of relatively elaborate procedures. For instance, it would mean routinely doing such examinations as bronchoscopy or gastroscopy in order to detect changes in the mucous membrane which have escaped other technics such as x-rays. It would mean air contrast barium-enemas to uncover lesions that were beyond the reach of the sigmoidoscope. Unfortunately for the individual, knowledge gained from this method

assures him only that he is free of one selected disorder at the time of the survey; he is given no assurance that the disorder cannot develop in his case at a later date. To avoid misunderstanding, I must stress once again that we are assuming that these conditions are completely symptomless. Naturally these elaborate procedures are justified whenever there is the slightest suggestion that pathology may be present in an individual case. Under such circumstances, nothing should be neglected to establish a diagnosis.

We can turn now to somewhat specific consideration of the problem of health examinations faced by the internist. As stated before, frequently the program is one consisting of the so-called "executive examinations." What are the desirable objectives? The number of examinations is relatively small, usually not over 1 to 5 per cent of the total employees of a corporation or organization. The average age is over 40 years. The incidence of chronic conditions in this age group is high enough to justify thorough exploration of all presenting symptoms. Statistically, the group is so small that case-finding techniques are not justified. An "executive" health examination program, therefore, encompasses the first three of our four objectives.

Expressed in familiar terms, the first objective, i.e., establishing rapport and friendly contact, roughly approximates the traditional "history." With the thought in mind, however, that the individual is essentially normal and healthy, emphasis can be placed on exploring job and personal life stresses, rather than on securing a detailed symptomatology of a specific disease process presented by an individual who is actually disabled.

The second objective, i.e., discerning the most recognizable physical defects, encompasses the careful physical examination. In dealing with a seriously ill person, the internist focuses his attention upon the mechanics of a specific disease process. Under those circumstances, such matters as overweight, poor posture, skin ailments, etc., are relegated to another day. In the executive examination, where, presumably, no serious disease is present, it is practicable to give careful consideration to matters which are not of immediate urgency but which, if corrected, would add materially to the happiness and productive efficiency of the individual.

The third objective, i.e., detecting chronic debilitating diseases, is extremely important to the executive. Probably one-half of 1 per cent of the general population has diabetes or a tendency toward it. It certainly is indicated to do a postprandial blood sugar on executives who generally are in the fifth decade of life. Likewise some arthritic conditions, localized due to previous trauma, or more generalized, are very frequently encountered. A definite diagnosis is helpful, as frequently the mind of the executive is relieved of the strain of considering dire conditions, such as cancer or heart disease, as the cause of his discomfort. Exactly what laboratory studies should be routinely carried out is a matter for the examiner to decide for himself. As a minimum, urinalysis, serologic test for syphilis, complete

blood count, sedimentation rate, x-ray of chest, nonprotein nitrogen, cholesterol, stool guaiac and electrocardiograph are suggested. The incidence of peptic ulcer or gastroduodenitis is high enough in this group to consider the inclusion of gastrointestinal x-rays. Sigmoidoscopy to detect papillomata is another valuable procedure.

In the periodic examinations which follow the original examination, the most important phase of the examination is the consultation between the examinee and the physician. Routine repetition of all procedures carried out at the original examination is not justified. A basic minimum of laboratory work should be done, and of course there should be a thorough laboratory investigation of any clue to disease uncovered by the interval history. It is my understanding that the Air Force, to conserve medical manpower, has established a "screening" examination, which replaces the old procedure where even a basic history was recorded year after year. This abbreviated examination includes a history in which emphasis is placed upon whether any new symptoms have appeared since the last survey. If so, these are investigated thoroughly and extensively, and with the use of every hospital and laboratory aid which is indicated. Otherwise, the examination consists of chest x-ray, urinalysis, hemoglobin, electrocardiography, dental inspection, rectal examination, examination of pelvis and of breasts (in females), and eye examinations.

The question of frequency of health examinations often comes up. The answer lies in the average age of the executives. If over 40, examinations certainly should be done annually. It must be stressed above all that regular calendar examinations must be supplemented by an understanding by the examinee that occurrence of symptoms of any kind deserves immediate investigation. It is natural that he should report to the physician who has last done a periodic health examination, and who has stressed to him that the periodic examination program detects long-run health trends rather than acute emergencies which are heralded by the appearance of new and unusual clinical symptoms. Finally, it must be stressed that the success of the program depends largely upon the thought, consideration and effort expended by the physician himself. This important factor must never be minimized in any program of periodic health examinations.

#### SUMMARY

1. Periodic health examinations contribute materially to day-by-day health by attention to minor deviations from the norm.
2. The original health examination should be a thorough health survey, with the determination of "base-line" laboratory and x-ray levels for future reference.
3. Subsequent examinations should stress health counseling and investigation of suspected conditions which have produced symptoms as elicited in an interval history.

4. Regular periodic examinations establish a rapport and understanding between examinee and physician that encourage the patient to report promptly new symptoms which occur between the dates of calendar examinations and which are worthy of clinical scrutiny and study.

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## CARCINOMA OF BODY AND TAIL OF PANCREAS \*

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### INTRODUCTION

A BRIEF survey of textbook descriptions concerned with the clinical picture produced by pancreatic carcinoma will usually leave the reader with the impression that neoplasia, other than in the head of the organ, is of extreme rarity. Indeed, Aird,<sup>1</sup> in a chapter of eight pages on carcinoma of the pancreas, dismisses growths of the body and tail in three lines. A similar neglect is apparent in the writings of many authors, and probably arises from the fact that until recently few attempts have been made to marshal the admittedly complex clinical features produced by growths in this site into a coherent syndrome. This attitude has resulted in an almost universal failure to recognize such cases during life. Although Chauffard<sup>2</sup> reported three examples in 1908, the first serious attempt to classify the manifestations of the condition was made by Duff,<sup>3</sup> who in 1939 reviewed 16 cases in which the diagnosis was confirmed at autopsy. Shortly afterwards Levy and Lichtman<sup>4</sup> reviewed 19 cases, and Russum and Carp<sup>5</sup> another eight, while recent reviews by Smith and Albright,<sup>6</sup> Brown et al.<sup>7</sup> and Thompson and Rodgers<sup>8</sup> have added further valuable information. From these studies it is apparent that carcinoma of the body and tail of the pancreas, though certainly less common than growths in the head, is a condition likely to be encountered in any general hospital and one that may give rise to serious difficulty in diagnosis. The finding of such tumors at autopsy, in clinically perplexing cases recently observed by the authors, suggested that a review of the clinical manifestations in a large series of cases might reveal features of diagnostic value leading to earlier recognition of the disease. Early diagnosis is by no means of academic interest only, since growths in the body and tail, if operable, are more easily removed than those in the head of the organ.<sup>1</sup>

### MATERIAL

This study is concerned with the clinical and pathologic findings in 58 cases of carcinoma of the body and/or tail of the pancreas. Tumors involving the whole gland, in which there was no evidence as to the site of origin of the neoplastic process, are excluded, but the series includes five cases in which the growth, clearly having arisen in the body, had infiltrated the head. The cases were discovered on scrutiny of the records of all medical and surgical admissions to the Royal Victoria Infirmary, Newcastle upon Tyne,

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during the 20 year period 1932-1951. The number of growths in the head of the organ occurring during the same period was noted, but these cases were not subjected to detailed analysis. The diagnosis in the cases of growth in the body or tail was confirmed at autopsy in 21 cases and at laparotomy in the remainder; additional confirmation was usually obtained in the surgical cases by biopsy. When no biopsy was taken the intra-abdominal findings left no doubt in the mind of the surgeon that there was a primary neoplasm in the pancreas. In several other cases explored operatively during the same period similar growths were probably present, but in view of Ingelfinger's<sup>9</sup> comment that diagnosis by laparotomy is occasionally unsatisfactory, all patients in whom there was any doubt of the diagnosis have been excluded from consideration.

#### INCIDENCE

During the period covered by this survey there were 347,614 admissions to this hospital; thus carcinoma of the body and tail of the pancreas occurred once in every 5,993 admissions. Two hundred and twenty-six cases of carcinoma in the head or whole organ were also seen during these years; thus the incidence of all pancreatic cancer was 0.82 per thousand admissions. No comparable statistics are available from published reports, although it has been suggested that carcinoma of the pancreas (including growths in the head) forms about 5 per cent of all cases of malignant disease.<sup>10, 11</sup> Duff<sup>8</sup> discovered 50 cases of primary pancreatic carcinoma in 14,000 autopsies carried out at The Johns Hopkins Hospital, an incidence of 3.6 per thousand autopsies, and of these, 19 growths were confined to the body and tail (1.36 per thousand). Hick and Mortimer<sup>10</sup> reported an incidence of 6.3 per thousand for all primary pancreatic neoplasms in a study of 7,932 autopsies at the Cook County Hospital, Chicago. The comparable figures from the present series are 39 cases of cancer of the head or whole organ and 21 growths in the body and tail in 9,167 autopsies; thus the incidence was 6.5 per thousand for all pancreatic cancer, and 2.3 per thousand for tumors confined to the body and tail.

#### LOCATION OF THE TUMOR

Duff<sup>8</sup> attempted to compare the incidence of growths in the body and tail of the pancreas with that in the head by listing the cases described in 14 reported series, including his own. He pointed out that the great variation between individual series could be accounted for by the fact that in some cases the diagnosis was clinical, in others it was made at autopsy. Clinical series tended to include a preponderance of neoplasms in the head, while pathologic series included an undue proportion of growths in the body and tail, many of which were unrecognized during life. This disproportion was accentuated by the fact that many patients with the clinical picture of carcinoma in the head of the organ were discharged from hospital and did

TABLE I  
Location of the Primary Tumor in Cases of Pancreatic Carcinoma

Author	Site of Growth						Total
	Head	Body	Tail	Body and Head	Body and Tail	Whole Gland	
Duff (1939)	28			19		3	50
Brown et al. (1952)	61	8	15	—	7	8	99
Thompson and Rodgers (1952)	107	14	9	3	10	14	157
Present series (all cases)	212	34	5	5	14	14	284
Present series (autopsy only)	35	9	4	1	7	4	60

not come to autopsy. Duff<sup>3</sup> concluded that approximately three times as many growths occurred in the head as elsewhere. The location of the tumor in the cases of the present series is compared with that noted in other reports in table 1. The figures in the series of Duff,<sup>3</sup> Brown et al.,<sup>7</sup> and Thompson and Rodgers<sup>8</sup> were all obtained from autopsy records; if the comparable cases of the present series are added it will be seen that, of 366 cases of carcinoma of pancreas found at autopsy, 260 growths arose in the head of the organ, and 106 were primary in the body and/or tail, a ratio of 2.5:1. However, when all cases of the present series are considered, including growths in the head or whole organ diagnosed clinically or at laparotomy, and cases of body or tail carcinoma recognized at operation, the ratio is 226:58, or approximately 4:1. Probably, for the reasons suggested by Duff,<sup>3</sup> the true incidence lies between these two figures and is about 3:1. Certainly this suggests that growths in the body and tail occur more commonly than is generally realized.

#### AGE AND SEX

Forty of the Newcastle cases (69 per cent) were males and 18 (31 per cent) were females; the youngest patient was a man of 33 years, the oldest a man of 73, and the average age was 56.8 years. The distribution of the patients by age and sex is given in table 2.

TABLE II  
Age and Sex Distribution of the Newcastle Patients

Age in Years	Number of Cases	
	Male	Female
30-39	2	1
40-49	9	2
50-59	13	8
60-69	12	5
70-79	4	2
Totals	40	18

There is no significant variation in the sex distribution of the condition at different ages. The figures given here agree broadly with the sex incidence in other reported series of carcinoma of all parts of the pancreas. Thus, Duff<sup>3</sup> reported 38 males (76 per cent) and 12 females (24 per cent), while Brown et al.<sup>7</sup> reported 72 males (72 per cent) and 28 females (28 per cent). In the series described by Thompson and Rodgers,<sup>8</sup> however, the male: female ratio was 1.5:1, and the sex incidence was actually equal in their colored patients. Comparing these figures with ours, it appears that the sex distribution of cancer of the body and tail of the pancreas does not differ from that of cancer elsewhere in the organ. The age incidence, too, is similar to that reported by other workers, although no case in the present series was so young as the 18 year old boy reported by Duff.<sup>3</sup> Smith and Albright<sup>6</sup> have given the average age of cases of carcinoma of the body and tail of the pancreas as 58.1 years, while in Duff's<sup>3</sup> cases of pancreatic carcinoma in any site the average age was 51.2 years. Comparison of these figures with the average of 56.8 years in the Newcastle series shows that the condition is most common in the sixth decade.

### CLINICAL FEATURES

#### A. SYMPTOMATOLOGY

1. *Duration:* The average duration of symptoms prior to admission to hospital was four and one-half months, the shortest history being two weeks, the longest two and one-half years. Thirty cases died in hospital, and the average duration of the illness from the first symptom until death was seven to eight months. These findings are similar to those of Brown et al., who found that in carcinoma in all parts of the pancreas, symptoms had been present for an average of four and one-tenth months before admission, and the illness lasted an average of seven and six-tenths months. The average

TABLE III  
First Symptom in Patients of the Newcastle Series

First Symptom	Number of Cases	Percentage
Abdominal pain	29	50%
Pain in back and side	9	15.5%
Severe constipation	2	3.5%
Diarrhea	2	3.5%
Vomiting	2	3.5%
Loss of weight	2	3.5%
Painful swollen legs (phlebothrombosis)	2	3.5%
Feverish illness	2	3.5%
"Abdominal swelling"	1	1.7%
Dysphagia	1	1.7%
Tiredness and weakness	1	1.7%
Epileptic seizure	1	1.7%
Lumps in the skin	1	1.7%
Breathlessness	1	1.7%
No information	2	3.5%
Total	58 cases	

TABLE IV  
Additional Important Symptoms Developing Before Admission

Symptom	Number of Cases
Abdominal pain which was not the first symptom	4
Hematemesis	4
Jaundice	3
Pain in the chest	1
Anorexia	1
Exhaustion	1
Diabetic coma	1
Dysphagia	1
Total	16

total duration in the autopsied cases of growths in the body and tail reported by Thompson and Rodgers <sup>8</sup> was nine and one-tenth months.

2. *First Symptom:* In Duff's <sup>3</sup> 16 cases, the most common initial symptoms were abdominal pain (14 cases), obstinate constipation (six cases), flatulence (six cases), swelling of the abdomen (five cases), and weakness (five cases). Anorexia and loss of weight were also prominent. Smith and Albright <sup>6</sup> in their 37 cases do not refer specifically to the first symptom; the cases reported by Brown et al.<sup>7</sup> and Thompson and Rodgers <sup>8</sup> cannot strictly be considered here, as these authors do not attempt to distinguish between the symptomatology of carcinoma of the head and that of growths in the body and tail.

The initial symptoms of the Newcastle patients are listed in table 3. It will be seen that, in general, these early symptoms correspond closely to those professed by Duff's <sup>3</sup> patients, excepting flatulence, which was not an initial complaint in any case of the present series. Individual symptoms will be considered in more detail shortly.

3. *Main Complaint on Admission:* Usually the dominant feature of the clinical history by the time the patient was admitted to hospital was the same as the initial complaint (table 3), but in 16 cases another symptom of later onset became dominant and compelled admission. These additional complaints are listed in table 4. It will now be convenient to analyze in detail all symptoms professed at the time of admission to hospital.

#### 4. Analysis of Symptoms:

(a) *Abdominal pain:* Forty-one patients (71 per cent) complained of pain in the abdomen. This symptom was present in 14 (87.5 per cent) of Duff's <sup>3</sup> cases, but in only 18 (48 per cent) of those reported by Smith and Albright <sup>6</sup>; it was, however, an outstanding feature in 73 (73 per cent) of the cases of carcinoma in all parts of the pancreas reported by Brown et al.<sup>7</sup>

(1) *Situation:* In 30 of the 41 cases the pain was situated in the upper abdomen; it was usually central, in the epigastrium, but in six cases it spread to the left side and was most severe in this situation, whereas in three cases it spread similarly to the right. Four patients had generalized abdominal

pain, while in seven others the pain occurred in the central or lower abdomen, being umbilical in four cases, hypogastric in one, in the right iliac fossa in one, and in the left iliac region in another.

(2) *Character and duration:* Pain was most commonly intermittent, although in 12 patients it was almost continuous; in three of these cases, however, occasional severe exacerbations occurred. The remaining patients had pain in attacks varying in duration from an hour or two to several days, and the nature of the pain was variously described as dull, aching, gnawing, gripping and nagging, although three patients had colicky pain and in one case it was stabbing. Often when an attack subsided a feeling of soreness remained. Two patients mentioned that they had upper abdominal discomfort which could not properly be regarded as pain.

The pain was made worse by the ingestion of food in 13 cases and was severe at night in another seven; it was intensified by cold in one case, by exertion in two, by defecation in one and by deep breathing in another. Relief was obtained by eructation in three cases, by taking alkalies in five, by eating or drinking in five, and by applying heat to the abdomen in four. Lying down gave relief in three cases, sitting up in another, while ease was obtained on defecation in two cases and after vomiting in one.

(b) *Pain in the back and chest:* Pain in the back occurred in a total of 21 cases. Seventeen of these cases also had abdominal pain, though in the majority the back pain was predominant. Sometimes pain in the abdomen seemed to go "through" to the back, but occasionally it traveled "round" the side. Factors which increased or relieved abdominal pain affected the back pain similarly. Pain was confined to the back and was severe in four cases, being constant and worse at night in three, but in one case it occurred in attacks. The pain was situated in the left scapular area in three cases, in the right scapular area in five, in the midlumbar region in six, and between the shoulders in seven.

Three patients had pain in the chest; thus, case 15 had substernal pain "like a lump," case 18 suffered attacks of pleuritic pain in the right side of the chest with no clinical or radiologic signs of pleural involvement, and in case 53 intermittent pain occurred in the left lower chest; however, this latter patient had previously suffered from a left-sided empyema.

Consideration of these data supports Duff's<sup>3</sup> assertion that "there is no constant type or location of pain which is common to all or even to a majority of the cases, much less any special characteristic of the pain which is peculiar to this disease alone." Whereas in most cases the pain is dull and intermittent in character and situated in the epigastrium, often with radiation to the back, these qualities are by no means invariable, and no specific precipitating or ameliorating factors have been noted. Duff<sup>3</sup> remarked that in all six of his cases in which the tumor was situated in the tail of the pancreas the pain radiated to the left side, but this was not noted in the present series. Not one of our five patients with growths in this site had left-sided pain;

two had epigastric pain radiating to the back and right shoulder, respectively, one had no pain, another had pleuritic pain in the right side of the chest, and the fifth had colicky upper abdominal pain. Chauffard<sup>2</sup> also emphasized that pain often began on the left and later moved to the midline and to the right, but this sequence was not observed in our cases. Smith and Albright<sup>6</sup> observed that the pain was relieved by sitting up and aggravated by lying down in 43 per cent of their cases, and Aird<sup>1</sup> has stressed that this is an important feature, often diagnostic of pain of pancreatic origin. Although in the present series pain was worse at night in 10 cases, when the patients were recumbent, there was no evidence that relief was obtained by sitting up; it was specifically noted in another three cases that lying down was effective.

Hence the information obtained from the Newcastle patients does not suggest that any constant type or situation of pain is typical of this disease.

(c) *Digestive symptoms:*

*Anorexia* was a prominent complaint, being mentioned by 37 patients (64 per cent). Sometimes it was long-standing and severe, and the loss of appetite was complete. One patient felt afraid to eat. In other cases loss of appetite was a recent complaint, occurring just before admission.

*Nausea* occurred in seven cases (12 per cent). It was a constant feature of the illness in three of these patients but in the others it came in waves in association with attacks of pain.

*Vomiting* was noted in 23 cases (40 per cent), but five of these patients had vomited only once. This symptom was rarely severe and usually of recent development; it does not appear to be a prominent feature of the disease. Hematemesis occurred in seven cases and will be considered shortly.

*Constipation* was described by 27 patients (47 per cent); it usually appeared within the few weeks prior to admission, but in several patients it was an early feature of the illness and became obstinate. This symptom has been stressed as of frequent occurrence,<sup>3, 6, 12</sup> and is also prominent in carcinoma of the head of the pancreas.<sup>8</sup> The mechanism of its production is obscure, and it must be remarked that in some cases of pancreatic carcinoma (11 per cent<sup>7</sup> or 19 per cent<sup>6</sup>), diarrhea may occur. It may be suggested that the latter symptom is more likely to occur in cases of growth in the head of the organ owing to excess fat in the stools, but it was noted in four of our cases (7 per cent) with growths in the body.

Other digestive symptoms of less prominence included *flatulence* (eight cases, 14 per cent), *heartburn* (three cases, 5 per cent), *abdominal distention* (six cases, 12 per cent), *postprandial dyspepsia* (four cases, 7 per cent), *abdominal tenderness* (one case) and *borborygmus* (one case). Abdominal distention was found to be due to ascites in every case; Duff<sup>3</sup> and Smith and Albright<sup>6</sup> have remarked on the frequency of this association.

(d) *Gastrointestinal hemorrhage:* Hematemesis and/or frank blood in

the stools was noted in nine cases (16 per cent), but in two of these patients it was probably unconnected with the primary disease, since one patient had bleeding piles and another diverticulitis of the colon. Hemorrhage in the remaining seven cases was considerable, and in four patients massive hematemesis and melena precipitated admission to hospital; in two of them bleeding was the immediate cause of death, and involvement of the gastrointestinal tract was demonstrated at autopsy. Thus, in case 19 a hard nodular mass was found in the body of the pancreas, infiltrating the tail; along the lesser curvature of the stomach were numerous mucosal deposits. A similar mass of growth was found in the body of the pancreas in case 20, but there were also numerous hemorrhagic submucous secondary deposits in the small intestine along the mesenteric border; a similar soft cushion of growth was seen on the greater curvature of the stomach, two inches from the esophagus and adherent to the tail of the pancreas. Barium meal studies were performed in four of these cases and were normal in two; gastroscopy also failed to reveal any abnormality in one case. However, in case 53 the barium meal suggested the presence of a gastric ulcer on the lesser curvature of the stomach; at laparotomy a mass in the body of the pancreas was adherent to the stomach at this point and was infiltrating to the mucosa. The barium meal in case 58 demonstrated a mass lying medial to the lesser curve and pushing the stomach forward.

In addition to these cases in which frank bleeding occurred, a further three showed persistent occult blood in the stools. In case 38, for instance, a barium meal revealed pyloric stenosis and gross deformity of the duodenum suggesting ulceration, but at laparotomy the stomach and duodenum showed extensive infiltration by growth and there was a primary neoplasm in the body of the pancreas. Case 44 presented as a case of esophageal obstruction; laparotomy revealed a mass in the body and tail of the pancreas extending to the esophageal hiatus of the diaphragm, where it was adherent to the diaphragm and stomach. Finally, a hypochromic anemia was noted in case 55, and occult blood was persistently present in the stools. Although barium studies and gastroscopy were negative, laparotomy revealed a carcinoma of the body of the pancreas, but there was no obvious infiltration of the alimentary tract.

It may be concluded that in at least 10 patients of the present series (17 per cent), gastrointestinal bleeding occurred and was severe in seven (13 per cent). Available evidence suggests that this complication is usually determined by infiltration of the alimentary tract either by the primary neoplasm or by secondary deposits. Duff<sup>3</sup> noted its occurrence in 50 per cent of his cases of carcinoma in the body or tail, but in only two cases (12.5 per cent) with growths in the head. It was observed in only one (3 per cent) of the series reported by Smith and Albright,<sup>6</sup> and in only three (2 per cent) of the cases of Thompson and Rodgers<sup>7</sup>; two of the latter patients had infiltration of the stomach and duodenum, and one had splenic vein throm-

bosis. Despite the infrequency of this event in the latter two reports, it appears that hemorrhage must be considered a significant feature of the clinical picture of this disease.

(e) *Loss of weight:* Fifty-one patients (88 per cent) mentioned that they had lost weight in the months prior to admission, and in 19 cases the loss was severe. For example, one patient had lost 42 pounds in three months, another 35 pounds in two months, another 49 pounds in five months, and yet another 28 pounds in one month. Analysis of these 19 cases revealed that a palpable mass was present in nine of them, and laparotomy or autopsy revealed the presence of metastases, often widespread, in every case.

Weight loss was described by all of Duff's<sup>3</sup> patients, and by 97 per cent of those reported by Smith and Albright.<sup>6</sup> It is also an important feature of carcinoma in the head of the pancreas, and Brown et al.<sup>7</sup> noted wasting in 94 per cent of their cases. However, there is a distinct impression, from study of the Newcastle patients and of those previously reported, that emaciation may be earlier and more profound in cases of body or tail carcinoma than in cases with growth in the head of the organ. This is probably due to the fact that jaundice occurs early in the latter cases and draws attention to the disease, whereas in patients with neoplasm in the body or tail weight loss may be severe before other prominent symptoms have developed.

(f) *Weakness and psychiatric manifestations:* A subjective feeling of weakness, tiredness or listlessness was described by 13 patients (22 per cent), all of whom had lost a considerable amount of weight. In one the sensation amounted to almost complete mental and physical exhaustion. Severe insomnia was also a prominent feature of the illness in two cases, and other patients mentioned episodes of depression, fear and excessive anxiety.

Extreme weakness, bordering on physical collapse, was noted frequently in the cases reported by Thompson and Rodgers,<sup>8</sup> and Brown et al.<sup>7</sup> remarked that severe fatigue and weakness were prominent in 54 per cent of patients with pancreatic growths in all situations. Yaskin<sup>13</sup> reported four patients in whom depression and insomnia and fear of impending disaster were early symptoms of pancreatic carcinoma, and Ulett and Parsons<sup>14</sup> remarked that 10 per cent of 87 cases presented as a psychiatric problem of some importance, usually with agitation and depression. Savage et al.<sup>15</sup> have recently considered in some detail the psychiatric manifestations of pancreatic disease. Twenty cases of proved pancreatic carcinoma were reviewed and in five cases, despite the presence of pain and weight loss, the symptoms were felt to be of functional origin. The pain in these cases was discounted by the physician because it appeared exaggerated, inconsistent or relieved by suggestion; only in three of the five patients was there evidence of previous emotional difficulties, and these three individuals also suffered from anxiety, sleeplessness and depression. The superficial resemblance of these symptoms to hysteria was pointed out. Weiss,<sup>16</sup> in discussing these cases, doubted whether carcinoma of the pancreas had specific psychologic

characteristics, and suggested that the physician's concern over the obscurity of the illness was probably reflected in the patient's anxiety. Whatever the explanation, there is no doubt that the bizarre nature of the early symptoms of this disease and the exaggerated descriptions of pain and weakness given by so many patients may lead to a diagnosis of functional disorder. At least two patients in the Newcastle series were regarded as hysterical owing to the exhibition of the above characteristics in the absence of physical signs, and it was only when cachexia became extreme that the possibility of malignant disease was entertained. Whatever the exact pathogenesis of symptoms of this nature, they may form a useful pointer to the diagnosis of cancer of the pancreas.

(g) *Jaundice*: Obvious jaundice was present on admission in seven cases (12 per cent), and developed a few days before death in a further four (7 per cent). It was present for less than a month in six cases, but had been noted for two to three months in one. Six patients showed a considerable degree of icterus, but in the other five it was mild; only one patient complained of pruritus.

Jaundice was similarly observed in eight (22 per cent) of the cases reported by Smith and Albright<sup>6</sup>; it was seen to a slight extent, relatively late in the course of the disease, in eight of Duff's<sup>3</sup> 16 cases (50 per cent). These findings are in marked contrast to those in cases of carcinoma of the head of the organ, when jaundice is an early and prominent symptom; it was initial in 13 of Duff's<sup>3</sup> 16 cases of carcinoma of the head.

The cause of the jaundice was evident at laparotomy or autopsy in all 11 Newcastle patients. In four there were neoplastic nodes in the porta hepatis, and in five, similar nodes or deposits of growth were found in the gastrohepatic omentum surrounding the common bile duct. In five of these nine cases the liver was massively infiltrated by secondary deposits. In another case cholangitis, cholangiectasis and distention of the gall-bladder were noted resulting from a simple stricture of the common bile duct in its intra-pancreatic portion, some distance away from the neoplasm in the body of the organ. Finally, a growth in the body of the gland in one patient had infiltrated the head and constricted the common bile duct. This patient had had abdominal pain and weakness for five months and jaundice for more than two; marked biliary cirrhosis was present at autopsy.

(h) *Other symptoms*:

*Swelling of the legs* prior to admission was noted in three patients (5 per cent) and was painful in two; in each case venous thrombosis was discovered. The incidence of this complication will be considered in more detail when the pathologic findings are related.

*Profuse sweating* was described by two patients, a symptom also noted by Smith and Albright.<sup>6</sup> Two patients were *comatose* on admission; in one there was an inadequate history, but he was said to have been comatose for

more than a week; at autopsy there was a growth in the body of the pancreas, with secondary deposits in the liver and both adrenals. A second patient was admitted in diabetic coma and showed some response to insulin treatment, but five days later signs of brain stem thrombosis developed and death supervened. At autopsy the majority of the body of the pancreas was occupied by a nodule of growth 5.5 cm. in diameter, and there were secondary deposits in the liver and adrenals.

One patient presented with *congestive heart failure* (auricular fibrillation, pulmonary and peripheral congestion) and died within a few hours. Autopsy revealed a carcinoma in the tail of the pancreas, with secondary deposits in the mediastinum, pleura, pulmonary root nodes, thyroid, liver and kidneys. Although the myocardium was fatty and the coronary arteries were atheromatous, the carcinomatosis probably played an important part in the production of cardiac failure.

In addition to the patient with brain stem thrombosis already mentioned, one other case presented with *neurologic symptoms*. This patient had a six months history of *grand mal* attacks, increasing in frequency; he was admitted in status epilepticus and died shortly afterwards. At autopsy there was a large firm tumor in the tail of the pancreas, with secondary deposits in the liver but none in the brain. An extract from the tumor gave a substance with an insulin-like action, and histologic examination suggested that this was an islet cell tumor.

*Breathlessness* was prominent in two cases, and in one of these it was marked only when an attack of upper abdominal pain developed. The second patient presented with a hypochromic anemia (hemoglobin, 32 per cent; 4.64 gm. per 100 ml.) and occult blood in the stools; a carcinoma of the body of the pancreas was found on laparotomy.

*Pallor* was remarked by one other patient, whose hemoglobin level was 38 per cent (5.51 gm. per 100 ml.) on admission; multiple secondary deposits were noted in the stomach wall in this case, arising from a carcinoma of the body and tail of the pancreas. Only in these two cases (3 per cent) were symptoms of anemia prominent, a finding which agrees with that of Levy and Lichtman<sup>4</sup>; Smith and Albright,<sup>6</sup> on the other hand, described the presence of anemia in 81 per cent of their cases. They do not, however, mention how often evidence of the anemia was discovered by the patient himself.

*Dysphagia* was the presenting symptom in two cases. Both patients showed evidence of severe weight loss, and in one a clinical and radiologic diagnosis of cardiospasm was made. In both cases a growth was discovered in the body and tail of the organ and was extending to the esophageal hiatus of the diaphragm, producing obstruction. This sequence of events does not appear to have been recorded previously.

In two cases *superficial swellings* were noted; one patient who developed painless lumps in the skin all over the body and had at first no other symp-

toms was found to have a carcinoma of the tail of the pancreas. The other patient developed a painful swelling, which proved on biopsy to be a secondary carcinoma, over the spine of the third lumbar vertebra; at autopsy there was an enormous mass in the body of the pancreas. Subcutaneous swellings were noted in two of the patients reported by Smith and Albright.<sup>6</sup>

Finally, it may be mentioned that one patient had a *constant desire to defecate*, but autopsy revealed no cause for this symptom.

#### B. PHYSICAL SIGNS

1. *Emaciation*: Loss of weight has already been considered as a symptom. On examination 41 patients showed sunken cheeks, lax, inelastic subcutaneous tissue, and other signs of weight loss; this evidence was particularly marked in 19 cases.

2. *Anemia*: Only nine patients (16 per cent) showed a significant degree of pallor of the skin, conjunctivae and mucous membranes. Two cases with severe hypochromic anemia have already been mentioned; the remaining cases had all suffered frank gastrointestinal bleeding. As suggested when the symptom of pallor was discussed, these findings are at variance with the high incidence of anemia reported by Smith and Albright.<sup>6</sup>

3. *Pyrexia*: Few patients admitted to symptoms of a febrile illness, and the temperature was raised above normal in only 16 cases (28 per cent) during the illness. In all but two of these patients there was a low grade, irregular pyrexia, never exceeding 100° F.; secondary deposits in the liver or elsewhere were discovered in most of them. Widespread metastasis has generally been adduced as the most common cause of fever in such patients, as in the three cases with high fever and drenching sweats described by Smith and Albright.<sup>6</sup> Brown et al.<sup>7</sup> noted fever in 26 of their cases of pancreatic carcinoma, exceeding 101° F. in 15 per cent and reaching 106° F. in a patient with widespread metastases. Our two patients with sustained high fever were found to have widespread thrombophlebitis and cholangitis, respectively; these are the two cases mentioned previously who suffered severe sweats. The available evidence suggests that many patients with carcinoma of the pancreas have no pyrexia; when the temperature is raised, fever is rarely excessive, save in the presence of widespread metastases or an inflammatory complication.

4. *Abdominal Mass*: An abdominal mass, invariably hard or firm and often nodular, was found on clinical examination in 26 cases (45 per cent). It was situated in the epigastrium in eight cases, in the right hypochondrium in 10, in the left hypochondrium in seven and in the skin of the abdominal wall in one. The mass was presumed to be hepatic in nine cases (three of those in the epigastrium and six of those in the right hypochondrium). In three patients a mass in the left hypochondrium was thought to be spleen, resulting in a diagnosis of leukemia in two cases and of subacute bacterial endocarditis in the other. In seven cases the swelling was presumed to be

neoplastic but the origin of the growth was not suggested; carcinoma of the stomach was suggested as the probable diagnosis in another four cases, and cancer of the colon in three.

Correlation of these clinical impressions with the findings at laparotomy or autopsy reveals that in nine cases (16 per cent) the palpable mass was in fact liver, enlarged owing to metastases in eight cases and to biliary cirrhosis in one. The spleen was not enlarged sufficiently to be palpable in any case, and the other 17 palpable swellings were either the primary tumor (10 cases, 18 per cent), or secondary deposits in the omentum and peritoneum (six cases, 10 per cent), or abdominal wall (one case, 2 per cent). These findings can be compared with those of Duff,<sup>3</sup> who found that the liver was palpable in 11 of his cases (69 per cent) and the spleen in four (25 per cent), whereas a tumor mass could be felt in only two cases (12.5 per cent).

5. *Superficial Metastases:* As already remarked, one patient showed multiple subcutaneous metastases over the chest and abdomen, and another had a large single deposit in the tissues overlying the spine of the third lumbar vertebra. No palpable deposits in lymph nodes were noted. Subcutaneous nodules were noted in single cases by Duff<sup>3</sup> and by Smith and Albright,<sup>6</sup> and Duff<sup>3</sup> also mentioned one case with involvement of a supraclavicular lymph node.

6. *Ascites:* Ascites was noted in seven cases (12 per cent); in six it was slight and barely detectable clinically, although five of the patients had experienced a subjective feeling of abdominal distention. In four of these cases peritoneal metastases were discovered, and in the other two neoplastic nodes were present in the porta hepatis and were probably obstructing the portal vein. One other patient, in whom multiple peritoneal deposits were found at autopsy, had a massive ascites and 15 pints of fluid were aspirated before death.

Duff<sup>3</sup> noted ascites in 10 of his cases (62 per cent), and abdominal distention, subsequently shown to be due to fluid accumulation, was an initial symptom in five patients. He gave reasons for suggesting that this sign was of relatively early occurrence and was much more common in carcinoma of the body or tail than in growths of the head of the pancreas. However, although fluid accumulated in 32 per cent of the cases reported by Smith and Albright,<sup>6</sup> it occurred relatively late in the course of the disease, and a similar event was noted in 28 per cent of the cases of carcinoma in all areas of the pancreas described by Brown et al.<sup>7</sup> Consideration of the findings in our cases does not support Duff's<sup>3</sup> conclusions; it is, however, confirmed that the presence of ascites usually means hepatic or peritoneal metastases, which are as likely to occur in carcinoma of the head as in growths in the body and tail.

7. *Abdominal Tenderness:* Tenderness on pressure, usually most marked in the epigastrium, was noted in 18 (33 per cent) of our cases; this sign was also a feature in 38 per cent of patients in the series of Smith and Albright.<sup>6</sup>

8. *Dilatation of superficial abdominal veins* occurred in three cases (5 per cent), and in one of these patients thrombosis of the common iliac veins was discovered at autopsy. Similarly, dilated venous channels were observed in two (12.5 per cent) of Duff's<sup>3</sup> cases and in four (25 per cent) of those reported by Ransom.<sup>12</sup>

9. *Abdominal distention* of moderate degree, due to accumulation of gas in the intestines, was apparent in four patients (17 per cent).

#### INVESTIGATIONS

The *urine* was examined in all cases and glycosuria was found in one only, the patient who was admitted in diabetic coma. Smith and Albright<sup>6</sup> found evidence of diabetes mellitus in three of their cases, and Brown et al.<sup>7</sup> found hyperglycemia in 10 of the 18 cases of pancreatic carcinoma in which the blood sugar was estimated. Although only one of our cases had glycosuria, no blood sugar estimations were performed, so that minor degrees of hyperglycemia may have escaped notice.

The *urinary diastase* was estimated in three cases only and was of no diagnostic value; no conclusions can be reached on so few cases. Unfortunately, the *serum amylase* was not estimated in any case.

In only two cases were the *stools* examined microscopically, and free fat globules were seen in both. Duff<sup>3</sup> does not refer to this investigation, and Smith and Albright<sup>6</sup> found evidence of pancreatic dysfunction in one case only. Brown et al.<sup>7</sup> have discussed the technic of stool examination in great detail, and have stressed its importance in the diagnosis of carcinoma of the pancreas. Abnormalities are more marked, however, with growths in the head of the organ, and are also found in other forms of pancreatic disease. The same objections can probably be raised in considering the value of estimation of the *blood lipase*<sup>17</sup> and the *secretin test*,<sup>18</sup> examinations which were not performed on the Newcastle patients. Nevertheless, it is probable that these investigations are worth while in suspected cases of pancreatic carcinoma.

The *blood* was examined in 20 cases only. In nine which have been referred to already, there was a significant degree of anemia, and one other patient had a hemoglobin level of 72 per cent (10.4 gm. per 100 ml.), in the absence of overt signs of bleeding. A leukocytosis (white blood cells, 10,000 per cubic millimeter) was discovered in seven cases; in one patient a count of 23,000 cells per cubic millimeter was recorded, and a preponderance of monocytes suggested a possible diagnosis of monocytic leukemia. The importance of leukocytosis has been stressed by Brown et al.<sup>7</sup> and by Arkin and Weisberg,<sup>11</sup> who noted that it was usually seen in patients with metastases.

*Analysis of gastric contents* was performed in nine cases and, in common with the experience of Brown et al.,<sup>7</sup> was found to be of no value. It gave a normal result in seven cases; in the other two patients there was achlorhydria, and free blood was present in the specimen examined.

Four patients were subjected to *gastroscopy*; in two no abnormality was noted, but the findings in the others indicated the need for laparotomy. Thus in case 21 there was free blood in the stomach, and an irregularity on the lesser curvature was seen; similarly, in case 25 an indurated area on the anterior wall of the stomach extending to the lesser curvature suggested malignancy, and at laparotomy a pancreatic growth was found to be adherent to the stomach at this point.

*Radiologic investigation* of the gastrointestinal tract was carried out in 20 cases. Thirteen patients had a *barium meal* alone, three a *barium enema*, and both investigations were performed in four cases. The barium meal was normal in eight cases (47 per cent), but some abnormality was detected in the remaining nine (53 per cent). Obstruction at the lower end of the esophagus was observed in two, being diagnosed as cardiospasm in one case and questionable simple stricture or extrinsic pressure in the other. A mass was noted in four cases (20 per cent), causing a filling defect in the stomach but apparently arising behind the organ; this mass produced pyloric obstruction in two. Deformity of the duodenal cap was noted twice (12 per cent); one of these patients had a previous history suggestive of peptic ulceration, but in the other, invasion of the duodenum by the neoplasm was demonstrated at autopsy. Finally, in one case an "ulcer crater" was demonstrated on the lesser curvature of the stomach; laparotomy showed that the wall of the stomach was infiltrated by growth at this point. The barium enema was normal in four cases; in one diverticulitis was revealed, in another a posteriorly situated mass was demonstrated but was also shown by barium meal. A filling defect suggesting colonic carcinoma was demonstrated at the pelvic junction in the remaining case. Thus, in only four cases (20 per cent) did these studies suggest pancreatic neoplasia, although abnormalities subsequently shown to be due to the growth were seen in a further four (20 per cent). Appearances suggesting duodenal ulceration (two cases) or displacement of the stomach (three cases) were noted by Smith and Albright<sup>6</sup> in a total of 17 per cent of those cases which were examined in this way. Brown et al.<sup>7</sup> noted abnormalities in 10 cases (28 per cent) of pancreatic carcinoma; the fact that duodenal obstruction or deformity was noted in half of them suggests that most of the responsible growths were situated in the head of the organ. However, in five (14 per cent) displacement of the stomach by an extrinsic growth was described. It will be seen that the percentage of abnormalities reported in the present series is greater than that noted elsewhere; probably suspicious radiologic findings may be expected in about 20 per cent of cases.

#### CLINICAL DIAGNOSIS

The correct clinical diagnosis was made in only three cases in our series, and this at a late stage of the illness. A similar experience has been reported by all other authors; thus, the diagnosis was incorrect in all of Duff's<sup>8</sup> cases

and was made on clinical grounds in at most four of the patients reported by Smith and Albright.<sup>6</sup> In both of these papers the authors list the many other presumptive diagnoses which were reached; usually, it is true, intra-abdominal malignancy was suspected, but various other conditions, varying from leukemia to prolapsed intervertebral disc or psychoneurosis, were considered in individual cases. These multiple diagnoses pay tribute to the pleomorphism of the clinical picture of this disease. In most patients in the Newcastle series an abdominal neoplasm was suspected; thus, carcinoma of the stomach was presumptively diagnosed in 11 cases, carcinoma of the colon in seven, carcinoma of the head of the pancreas in two, and carcinoma of the esophagus in one. Other diagnoses suggested included leukemia (two cases), peptic ulcer (three cases), hysteria (two cases), functional dyspepsia, cirrhosis of the liver, cardiospasm, subacute bacterial endocarditis, congestive heart failure, thrombophlebitis, lumbar fibrositis, liver abscess, epilepsy and diabetic coma.

#### PATHOLOGIC FINDINGS

As already mentioned, 21 cases came to autopsy, and in the remaining 37 the diagnosis was confirmed at laparotomy. The situation of the primary growth has been noted in table 1. Attempts to correlate the clinical findings with the situation of the tumor have not revealed any significant associations; for instance, it was noted that left-sided pain did not occur in growths beginning in the tail, and this symptom occurred in only one case, in which a growth in the body had infiltrated the tail. It may be concluded that the clinical findings do not vary significantly, whether the growth arises in the body or in the tail of the organ.

*Spread of the Growth:* This must be considered under two headings; first, the surgical cases, in which only the intraabdominal spread can be recounted; and second, the autopsied cases, in which it is possible to assess more accurately the extent of metastasis.

TABLE V  
Intraabdominal Metastases in 37 Cases

Situation of Metastases	Number of Cases	Percentage
None	8	22%
Regional lymph nodes (pancreatic, preaortic, para-aortic, celiac, prepyloric, portal fissure, omental)	18	49%
Liver (invariably multiple)	14	38%
Greater omentum	3	8%
Lesser omentum	3	8%
Stomach	3	8%
Mesentery of small bowel	4	11%
Peritoneum (most marked in pelvis)	3	8%
Spinal column	2	5%
Diaphragm	2	5%
Colon	1	3%
Duodenum	1	3%
Small bowel	1	3%

TABLE VI  
Situation of Metastases in 21 Autopsied Cases

Situation	Number of Cases	Percentage
Abdominal lymph nodes	17	81%
Portal fissure	5	
Para-aortic	4	
Preaortic	2	
Celiac	3	
Lesser omentum	3	
Pancreaticoduodenal	2	
Retroperitoneal	1	
Along lesser curve of stomach	3	
Iliac	1	
Mesenteric	1	
"Abdominal"	3	
Liver	15	71%
Parietal peritoneum	2	10%
Greater omentum	3	14%
Lesser omentum	1	5%
Gall-bladder	4	19%
Stomach	6	29%
Esophagus	2	10%
Colon	1	5%
Mesentery	1	5%
Small bowel	1	5%
Kidneys	2	10%
Adrenal (bilateral in 3)	6	29%
Ureter	1	5%
Common bile duct	1	5%
Diaphragm	1	5%
Hilum of spleen	1	5%
Ovary	1	5%
Testis	1	5%
Prostate	2	10%
Bones	4	19%
Lumbar vertebrae	2	10%
Sternum	1	5%
Mandible	1	5%
Thoracic contents	8	38%
Lung	1	5%
Myocardium	2	10%
Pleura	2	10%
Mediastinum	2	10%
Bronchopulmonary nodes	1	5%
Thyroid gland	2	10%
Parotid gland	1	5%
Inguinal lymph nodes	1	5%
Subcutaneous tissues	1	5%

1. *Laparotomy*: Of 37 cases there was no evident intraabdominal spread in eight, but the primary growth was considered inoperable in all. Possibly with modern surgical technics some of these tumors could have been removed. The extent of the intraabdominal spread in the other patients is given in table 5. The direction of dissemination did not appear to depend upon the situation of the primary growth, save for the fact that diaphragmatic metastases occurred only in growths involving the tail, a point previously noted by Brown et al.<sup>7</sup>

2. *Autopsy*: Only one of the 21 cases which came to autopsy showed no evidence of spread of the lesion beyond the pancreas. The distribution of secondary deposits in the other cases is given in table 6.

Usually the abdominal lymph nodes involved were those in the upper abdomen, but in three cases the spread was very extensive. In all cases with hepatic involvement the deposits were multiple, varying in size from a pin-head to a mass 11 by 8 cm. in diameter; the deposits were usually yellowish white and were often hemorrhagic or umbilicated. Many were seen to be in a periportal distribution, indicating blood spread, but there was no preponderance in the left lobe of the organ. Massive deposits in abdominal lymph nodes or the greater omentum were responsible for the palpable tumor observed clinically in six cases. The deposits in the gall-bladder involved the peritoneal surface in only three cases but had infiltrated the mucosa in one. The stomach showed multiple submucosal infiltration in two cases, with superficial ulceration in one; in the remaining four patients a cushion of tumor had infiltrated the wall massively but apparently had not penetrated the mucosa. Infiltration through the esophagus had occurred at the cardiac orifice in one case, and, as already mentioned, a diaphragmatic deposit had caused compression at this point in another, although the esophagus was not itself involved; however, in an additional case the gullet was narrowed by an infiltrating metastasis at the level of the tracheal bifurcation, but this patient had not complained of dysphagia.

The distribution of the metastases in this series agrees broadly with the figures given by Duff<sup>3</sup> for the spread of carcinoma in the body and tail of the organ, although more extensive extraabdominal spread was noted in our cases. He discussed the subject in great detail, pointing out that spread occurred via perineural spaces, lymphatics and veins. The distribution of the deposits is also in general agreement with the findings of Brown et al.<sup>7</sup> and Thompson and Rodgers<sup>8</sup> for cases of neoplasm in all parts of the pancreas, save for the incidence of deposits in the duodenum and lungs. As would be expected, duodenal infiltration is more common in cancer of the head of the organ, and was not seen in our cases at autopsy. Brown et al.<sup>7</sup> suggested that spread to the lungs was twice as common with growths situated in the body or tail as with those in the head, and Thompson and Rodgers<sup>8</sup> noted spread to the lungs in 23.6 per cent of their cases. These findings are not substantiated by our experience, nor did we note the high incidence of peritoneal and pleural effusions described by Thompson and Rodgers,<sup>8</sup> although the two cases with deposits in the parietal peritoneum and one of the two with pleural deposits showed some fluid accumulation.

*Vascular Thrombosis:* Thrombotic changes in arteries or veins were discovered at autopsy in six cases (29 per cent). None of the cases diagnosed at laparotomy showed clinical evidence of thrombosis, but, on the other hand, such signs were present in only three of the cases in which extensive vascular changes were found at autopsy.

Two patients (cases 6 and 45) presented with a typical clinical picture of thrombophlebitis migrans. Each had pain, swelling, tenderness and discoloration of the legs, with fever and leukocytosis, and the illness ran a

remittent course, with two attacks of pulmonary infarction in one case and cerebral and pulmonary episodes in the other. In each case peripheral and visceral venous thrombosis, as well as arterial thrombosis, was discovered at autopsy. Veins affected included the external jugular (one case), both femorals and common iliacs (both cases), and arterial thrombosis with infarction occurred in the lungs and spleen in both and in the renal and coronary vasculature in one. The third patient with clinical evidence of vascular pathology developed the typical syndrome of posterior inferior cerebellar artery thrombosis and also had a swollen left leg. At autopsy the left femoral and external iliac veins were thrombosed, and there were multiple infarcts in the lungs and spleen.

One of the remaining three patients in whom the presence of vascular thrombosis was not recognized during life suffered an acute feverish illness with night sweats and leukocytosis, and a diagnosis of subacute bacterial endocarditis was suggested; at autopsy there was thrombosis of the inferior vena cava, both common iliac and femoral veins and the left renal vein. Thrombosis was mainly visceral in the remaining two cases, involving the portal vein in one and the portal, superior mesenteric, hepatic and femoral veins in the other.

Widespread metastases were noted in all six of these patients with vascular involvement, but only in the two with portal vein thrombosis could it be suggested that thrombosis was due to pressure upon the vein by growth or tumor emboli. The primary growth was situated in the body of the organ in two cases, in the tail in two and in the body and tail in two.

Many authors have stressed the relationship between multiple thrombosis and carcinoma of the pancreas. Sproul<sup>19</sup> found that 31.3 per cent of cases of carcinoma in the body and tail showed multiple venous thrombi, whereas this was true of only 2.5 per cent of cases of bronchogenic carcinoma and 1.3 per cent with gastric neoplasia. Similar findings were reported by Kenny,<sup>20</sup> who found multiple venous thrombi in 33 per cent of cases of growth in the body or tail, and no multiple thrombi in patients with growths in the head. Thompson and Rodgers,<sup>8</sup> however, showed that multiple thrombi may be found when the tumor arises in the head, though with less than half the frequency found when it is primary in the body or tail. Multiple thrombi occurred in five (24 per cent) of our autopsied cases, an incidence somewhat lower than that reported by Sproul<sup>19</sup> and Kenny<sup>20</sup> but agreeing with the 22 per cent of Smith and Albright.<sup>9</sup> This may be due to the fact that Sproul<sup>19</sup> and Kenny<sup>20</sup> concentrated particularly on vascular thrombosis, whereas some examples may have been missed in our series. For this reason, too, the cases which did not come to autopsy have not been considered. It is evident, however, that signs of multiple vascular thrombosis were the presenting feature of the illness in at least three of our cases; this confirms the suggestion made by other authors that thrombophlebitis migrans, in the absence of any apparent cause, should compel a search for other evidence of pancreatic carcinoma.

The cause of the widespread thrombosis is as yet unknown. Sproul<sup>19</sup> suggested that the tumor cells increased the trypsin content of the circulating blood and so promoted clotting, while Kenny<sup>20</sup> also postulated the secretion of a clot-promoting substance, pointing out that in his cases with multiple thrombi the tumor cells showed mucoid change. It is of interest that mucoid change was noted histologically in only three tumors in our series, and all three patients showed multiple thrombi at autopsy. Recent work by Moolten et al.<sup>21</sup> has added further evidence along these lines; they suggest that thrombocytosis, which increases platelet adhesiveness, is often a by-product of necrosis within a tumor. This substance, together with increased production of pancreatic lipase, may cause intravascular platelet coagulation and so promote clotting. This work has yet to be confirmed.

*Histology:* The histologic appearances in pancreatic body and tail carcinoma closely resemble the findings in growths of the head and have been discussed in detail by Duff<sup>2</sup> and others. Information available concerning the findings in 19 of our cases does not add to that given in previous reports. In every case save that with an islet cell tumor the growth was adenocarcinomatous in type; four showed a desmoplastic reaction and three mucoid change.

#### CONCLUSIONS

The extreme variability of the clinical picture in the cases reported and the comparative inutility of investigational methods readily explain the low proportion of accurate clinical diagnoses reached in cases of carcinoma of the body and/or tail of the pancreas. It is also clear that in a proportion of cases clinical diagnosis will never be possible before the tumor has spread so widely as to be inoperable. Nevertheless, the only hope of successful treatment lies in early diagnosis, and it is suggested that certain clinical pointers exist which may raise the suspicion of neoplasia in this situation.

Abdominal pain is characteristically intermittent and somewhat dull in character, though it is occasionally severe; it is usually epigastric in situation, and frequently radiates to the back but not often to the left side. It is often worse at night but does not show the characteristic features of peptic ulcer pain. We have not found it to alter significantly with change of position. Quite often it is described in glowing, exaggerated terms, and this may suggest a functional basis, particularly if there are associated overt anxiety and depression; in any such case the possibility of pancreatic carcinoma should be kept in mind, especially if loss of weight has occurred. Anorexia and severe weight loss are often early symptoms, but even more characteristic is a subjective feeling of weakness or exhaustion, rarely met with so early in the course of other intraabdominal malignant disease. Vomiting is not prominent, but obstinate constipation is frequent; gastrointestinal bleeding occurs significantly often but is usually of late onset, due to infiltration of the gastrointestinal tract; hence this symptom cannot be considered useful in early recognition of the disease. Jaundice, in contradistinction to

cases with growths in the head of the organ, is uncommon and also occurs late, indicating metastasis, as does ascites. Anemia appears to be of little significance, while the presence of an abdominal mass usually suggests that the disease has progressed beyond effective aid. Most important, however, is the occurrence of thromboembolic manifestations, particularly if multiple; the combination of any of the vaguer symptoms and signs related above should lead to a careful search for evidence of thrombosis which, once found, may suggest pancreatic neoplasia as the source of symptoms. Under such circumstances, too, a battery of investigations, including examination of the blood and estimation of the urinary diastase, serum amylase and blood lipase, as well as the secretin test, may be indicated. More important still, the stools should be carefully examined for free or excess fat or undigested protein, and a barium meal examination should be performed with particular attention to the position and shape of the stomach and the relations of the duodenum. However, even though each of these investigations is occasionally helpful, none is infallible, and certain diagnosis can be achieved only by laparotomy. This is the next logical step, and even if occasional unnecessary operations are performed, this will be justifiable if a proportion of patients with early pancreatic carcinoma are saved.

It cannot be suggested that the features outlined will allow a correct diagnosis to be reached in every case. Many of our cases were beyond surgery when their first symptoms (dysphagia, or lumps in the skin, for instance) appeared. However, it is probable that appreciation of the occasional significance of weakness, exhaustion, thrombotic manifestations and abdominal pain of the type described may lead to earlier diagnosis and possibly effective surgery.

#### SUMMARY

Fifty-eight cases of carcinoma of the body and/or tail of the pancreas are reported; the diagnosis was made at laparotomy in 37 cases, at autopsy in 21. The condition occurred approximately once in every 6,000 admissions to the Royal Victoria Infirmary over a 20 year period. The incidence of the cases coming to post mortem was 2.3 per thousand autopsies. Forty of the patients were male (69 per cent), 18 female (31 per cent); the average age was 56.8 years.

The primary growth was situated in the body of the organ in 34 cases, in the body infiltrating the head in five, in the body and tail in 14, and in the tail in five.

Symptoms had been present for an average of four and one-half months before admission, and in 30 cases the average total duration of the illness was seven to eight months.

Prominent symptoms were pain (71 per cent), anorexia (64 per cent), loss of weight (88 per cent) and subjective feelings of weakness or exhaustion (22 per cent); the clinical picture of thrombophlebitis migrans occurred in three cases. Pain was characteristically intermittent and epigastric in

situation; severe back pain was also common. Left-sided pain was not a characteristic feature, nor was pain altered significantly by change in posture, although in several cases it was worse at night. In two cases exaggerated descriptions of the pain, combined with anxiety and depression, suggested a diagnosis of functional disorder. Gastrointestinal hemorrhage, severe in seven cases, occurred in 10 patients (17 per cent) but was a late manifestation due to infiltration of the gastrointestinal tract. Jaundice, too, occurred late in seven cases (12 per cent), owing to dissemination of the growth. Several patients were symptom-free until symptoms due to metastases (abdominal distention due to ascites, dysphagia or multiple subcutaneous nodules) made their appearance.

Forty-one patients showed evidence of weight loss on admission, and this was severe in 19. Anemia was noted in nine cases (16 per cent), but was usually due to frank bleeding. Pyrexia occurred in only 16 cases (28 per cent) and was usually of low grade, although high fever developed in two cases with inflammatory complications. An abdominal mass was felt in 26 cases (45 per cent); it was shown to be due to hepatic enlargement in nine cases (16 per cent), the primary growth in 10 (18 per cent) and metastases in omentum or lymph nodes in six (10 per cent). Superficial metastases were recognized in two cases (3 per cent), and ascites, invariably due to dissemination of growth, occurred in seven (12 per cent).

Leukocytosis was observed in seven of the 20 cases in which the blood was examined, and suggested a diagnosis of leukemia in one. Diabetes mellitus occurred in one case only. Radiologic studies of the gastrointestinal tract suggested pancreatic neoplasia in four cases (20 per cent of those examined), and gave appearances later shown to be due to growth in another four. Stool examination, the secretin test and estimations of urinary diastase, serum amylase and blood lipase were not carried out sufficiently often to be of value in our patients, but should probably be performed in suspected cases.

The clinical diagnosis was correct in only three cases, and although intraabdominal malignancy was suspected in many, numerous other diagnoses were suggested.

Study of the pathologic findings did not suggest that the clinical picture varied significantly with the situation of the neoplasm within the pancreas. Metastasis occurred most commonly to regional lymph nodes, liver, omentum, gastrointestinal tract, adrenals and bones, but many other organs were occasionally involved. Multiple vascular thrombi were noted in five of the autopsied cases (24 per cent).

It is concluded that in the presence of the clinical features described, and even if multiple investigations are negative, laparotomy may be indicated. In many cases the primary growth will be inoperable before significant symptoms appear, but in others laparotomy on suspicion may confirm the diagnosis and lead to successful treatment.

## ACKNOWLEDGMENT

We are grateful to the physicians and surgeons of the Royal Victoria Infirmary for permission to consult their records and to report data obtained from their cases. Our thanks are also due to Professor J. B. Duguid for allowing us access to the records of the Department of Pathology. We are also indebted to Mr. C. F. Naylor and to the staff of the Records Department for their help, and to Mrs. J. Molyneux for assistance in preparation of the manuscript.

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## ELECTROCARDIOGRAPHIC CHANGES DURING HEMODIALYSIS, WITH OBSERVATIONS ON CONTRIBUTION OF ELECTROLYTE DIS- TURBANCES TO DIGITALIS TOXICITY \*

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EXTRACORPOREAL hemodialysis is often lifesaving in the treatment of acute renal insufficiency, but the procedure itself is not without danger. Heparinization may be accompanied by hemorrhage; the patient may accidentally undergo in a short period of time a net gain or loss of blood volume from or into the machine<sup>1</sup>; elevation of blood pressure may occur,<sup>2</sup> and cardiac arrhythmias may be produced. In the course of observations on these cardiovascular changes during 13 consecutive hemodialyses with a Kolff type dialyzer at the Albany Hospital, electrocardiographic changes were noted in 11 instances and arrhythmias in three. It was felt that such frequent alteration of cardiac activity warranted more detailed analysis.

### MATERIALS AND METHODS

Hemodialysis was carried out with a so-called "Brigham-modified Kolff artificial kidney," described elsewhere.<sup>3</sup> A Sanborn direct writing electrocardiograph was used to record standard and unipolar limb leads and Lead V<sub>4</sub> every half hour during the dialysis. The electrode was applied to the shoulder of the extremity to which the arterial and venous cannulas were attached.

Serum sodium and potassium determinations were performed by means of an internal standard flame photometer, and calcium was determined by the method of Larson and Greenberg.<sup>4</sup>

### CASE REPORTS

*Case 1.* B. A. F., a 17 year old schoolgirl, entered the hospital on November 28, 1951, because of renal failure. She had been ill for about one month with fever, anemia, hematuria and ankle edema. Her urine volume had been falling and her nonprotein nitrogen rising. She was a well developed girl with a puffy, pallid face and a macular rash over her cheeks. Temperature was 99.2° F.; pulse, 72; respirations, 18; blood pressure, 130/94 mm. of Hg. She was in no acute distress, and 1 plus ankle edema was the only noteworthy physical finding. Hematocrit was 24;

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white blood cell count, 3,000, with a normal differential. Urine: acid; specific gravity, 1.019; protein, 4 plus; microscopic, innumerable white and red cells and frequent hyaline and granular casts per high power field. Because of uremia, nausea, vomiting and potassium intoxication, hemodialysis (BAF-1) was carried out for seven hours. The procedure was uneventful except for a rise in blood pressure from 110/60 mm. of Hg to 180/100 mm. of Hg, which was reduced by 0.25 mg. of Veriloid intravenously at the end of the fifth and seventh hours. Hemodialysis altered the serum sodium from 134 to 140 mEq./L.; potassium fell from 8.6 to 4.7 mEq./L.; calcium rose from 2.5 to 5.1 mEq./L.; bicarbonate, 16 to 18 mEq./L.; chloride, 104 to 102 mEq./L.; nonprotein nitrogen, 183 to 63 mg. per cent; and creatinine, 11.2 to 5.0 mg. per cent. The electrocardiogram at the start showed tent-shaped T waves which became rounded and lower during dialysis. The patient felt better the day after dialysis, and thereafter was able to take about 1,100 calories daily of a sodium, potassium and protein-free diet. Although the daily urine volume varied from 0 to 175 c.c., there was no appreciable rise in nonprotein nitrogen or creatinine over a period of one month. On the thirty-first hospital day, however, the patient suddenly complained of headache and loss of vision. A short time later she died in coma. Autopsy was refused.

*Case 2.* L. C., a 26 year old housewife, entered the hospital on December 28, 1951, because of anuria for three days following a premature separation of the placenta. Two previous pregnancies had been uneventful except for urinary tract infection. Her third and present pregnancy was also marred by hypertension. At delivery, hemorrhage resulted from premature separation of the placenta, and the patient was transfused with a liter of correctly matched blood. On entry the patient was a pale young white woman in no distress who showed the usual postpartum physical findings. Temperature, pulse and respiration were normal, but her blood pressure was 174/96 mm. of Hg and the fundi displayed Grade III hypertensive retinopathy. The hemoglobin was 5 gm. per cent; white count and differential, normal; urine: cloudy, acid reaction; specific gravity, 1.010; protein, 3 plus; microscopic, many white and red cells with a rare granular cast per high power field. Two episodes of severe pulmonary edema occurred the day after entry and the patient was digitalized and given 2 c.c. of Digalen daily.

On January 2, 1952, hemodialysis (LC-2) was carried out for six hours and during dialysis the lungs became free of râles. A rise of blood pressure to 220/120 mm. of Hg was reduced by Veriloid, 0.88 mg. and 0.36 mg. intravenously on two occasions. Dialysis produced the following blood chemical changes: sodium, 153 to 145 mEq./L.; potassium, 8.0 to 5.2 mEq./L.; calcium, 4.2 to 7.3 mEq./L.; bicarbonate, 16.0 to 15.6 mEq./L.; chloride, 96.0 to 99.0 mEq./L.; nonprotein nitrogen, 190 to 69 mg. per cent; creatinine, 15.5 to 6.6 mg. per cent. The cardiogram which initially showed ST depression and poor T waves over the left precordium, interpreted as digitalis effect and left heart strain, underwent an increased ST depression and T wave elevation which was consistent with an increased digitalis effect. There was prolongation of the QT<sub>c</sub> following Veriloid.

On January 10 hemodialysis (LC-4) was again performed. Four hundred cubic centimeters of blood were given during the procedure to correct anemia. Serum sodium was altered from 139 to 143 mEq./L.; potassium, 6.9 to 4.6 mEq./L.; calcium, 3.4 to 5.5 mEq./L.; bicarbonate, 15 to 17 mEq./L.; chloride, 86.0 to 104 mEq./L.; nonprotein nitrogen, 210 to 75 mg. per cent; and creatinine, 16.5 to 7.2 mg. per cent. The cardiogram, which again initially showed ST depression and lowered T waves over the left precordium, interpreted as left heart strain and digitalis effect, underwent a marked increase in ST depression, with loss of T waves and increasingly frequent premature auricular contractions, until runs of paroxysmal auricular tachycardia occurred as shown in figure 1. That this tachycardia caused a decrease in

cardiac output was suggested by the fall in blood pressure from 180/100 to 150/70 mm. of Hg, associated with a marked drop in blood flow from the radial artery into the artificial kidney. The run was stopped after five hours because of this apparently increasing digitalis intoxication. The cardiographic changes are shown in figure 1.

After 13 days of severe oliguria, and a stormy course marked by an emergency hysterectomy and a severe fungus infection, the patient reestablished improved kidney function and was discharged on January 31, 1952, with hypertension and Grade III hypertensive retinopathy. Since discharge her hypertension has gradually decreased.

*Case 3.* D. L., a 25 year old salesman, entered the hospital on January 7, 1951, because of potassium intoxication. He had been in robust health until two months

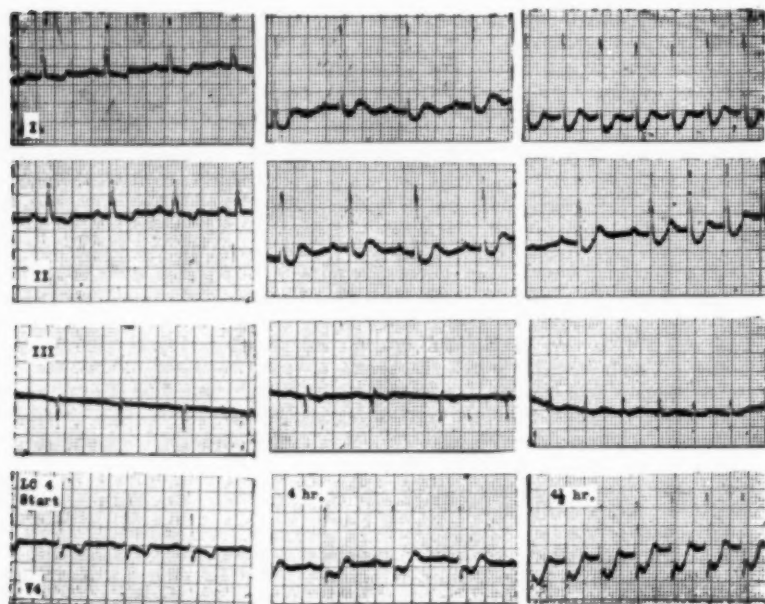


FIG. 1. Electrocardiographic changes during dialysis LC-4, showing evidence of increasing digitalis effect after four hours and paroxysmal auricular tachycardia 30 minutes later. Normal sinus rhythm breaks through for a few beats in Lead II.

before admission, when he became ill with fever, albuminuria, oliguria, face and ankle edema, nose-bleeds and, more recently, hypertension with blurring of vision. He was found on entry examination to be a large man who had a yellowish, pasty, puffy face and who complained of constant nausea. Temperature and respirations were normal, but the blood pressure was 180/100 mm. of Hg and the heart rate, 50. Grade III hypertensive retinopathy was present. There was marked edema of the back and lower legs. The hematocrit was 35 per cent; the white blood cell count and differential, normal. Urine: acid; specific gravity, 1.012; protein, 4 plus; red cells, 10 to 12; white cells, 1 to 4, and many hyaline and granular casts per high power field. Hemodialysis (DL-3) was carried out uneventfully for six hours on January 7 for potassium intoxication, although glucose and insulin given intravenously had reduced

somewhat the high K level on admission. Blood chemical changes were as follows: sodium, 127 to 137 mEq./L.; potassium, 7.7 to 4.6 mEq./L.; calcium, 4.9 to 5.1 mEq./L.; bicarbonate, 13 to 21 mEq./L.; chloride, 86 to 97 mEq./L.; nonprotein nitrogen, 152 to 80 mg. per cent; and creatinine, 13.3 to 7.7 mg. per cent. The cardiogram, which was within normal limits at the start, showed a lowering and rounding of all T waves during dialysis.

Very slowly over a period of 35 days the patient lapsed further into uremia, and hemodialysis (DL-6) was again performed for six hours on February 11. Blood pressure elevations to 220/130 mm. of Hg were reduced by Veriloid, 0.70 mg. intravenously on three occasions. Blood chemical changes were as follows: sodium, 140 to 140 mEq./L.; potassium, 7.3 to 4.5 mEq./L.; nonprotein nitrogen, 212 to 98 mg. per cent; and creatinine, 15.3 to 9.3 mg. per cent. The cardiogram again showed lowering of the T waves. The day following dialysis the patient had several severe convulsions, lapsed into coma, and died on February 19. Postmortem findings were characteristic of subacute glomerular nephritis and hypertension. The heart demonstrated only marked left ventricular hypertrophy.

*Case 4.* V. M., a 29 year old woman, entered on February 8, 1952, because of coma and convulsions. One week before entry she had used carbon tetrachloride for cleaning in a closed room and this had been followed by vomiting, oliguria and, later, convulsions and coma. On admission the patient was comatose but very restless. There was some edema of the back. Temperature, pulse, respirations, blood pressure and physical examination were within normal limits. Red blood cell count, white blood cell counts and differential, and liver function tests were normal. Lumbar puncture demonstrated normal cerebrospinal fluid. The urine, however, was packed with red cells and granular casts and showed a 3 plus protein.

Hemodialysis (VM-5) was performed on February 8 because of severe electrolyte derangement. A rapid correction of sodium concentration from 112 to 136 mEq./L. was associated with a fall of hematocrit from 45 to 33, a blood pressure rise from 140/70 to 190/70 mm. of Hg, and the appearance of râles throughout the lung fields, but the cardiogram remained within normal limits. The over-all blood chemical changes were as follows: sodium, 112 to 141 mEq./L.; potassium, 4.2 to 4.9 mEq./L.; calcium, 3.9 to 6.1 mEq./L.; bicarbonate, 10 to 8.2 mEq./L.; chloride, 76 to 77 mEq./L.; nonprotein nitrogen, 110 to 49 mg. per cent; creatinine, 9.8 to 4.7 mg. per cent. Consciousness returned shortly after dialysis and convulsions did not recur.

Hemodialysis (VM-7) was performed again on February 17, and elevation of blood pressure to 220/90 mm. of Hg was reduced by 0.80 mg. of Veriloid intravenously on two occasions. The chemical changes were as follows: sodium, 135 to 140 mEq./L.; potassium, 4.7 to 4.0 mEq./L.; calcium, 2.9 to 6.2 mEq./L.; bicarbonate, 6.5 to 19 mEq./L.; chloride, 98 to 104 mEq./L.; nonprotein nitrogen, 136 to 59 mg. per cent; creatinine, 15.7 to 5.6 mg. per cent. The cardiogram showed poor T waves throughout, worse over the left side of the heart, which were not altered by dialysis and which were interpreted as left heart strain. The urine output reached 1 L. 14 days after the onset of oliguria and the patient was discharged, apparently well, on February 27.

*Case 5.* M. N., a 56 year old housewife, entered on February 23 because of anuria for one day. She had had heart disease with auricular fibrillation for many years, but by using digitalis and restricting salt had remained compensated. During the four days before the onset of anuria she had been troubled by episodes of sudden, severe pain in the right and left flanks, with hematuria and cylindruria. Genito-urinary studies had revealed no cause for the anuria. She was found on entry to be a dark-skinned woman, severely ill and in considerable pain. Vital signs were within normal limits. Examination also disclosed enlargement of the heart to right and

left, a precordial heave, a completely irregular rhythm, and a snapping first sound at the apex. The lungs were clear but the abdomen was diffusely distended, tympanitic and somewhat tender. Hemoglobin was 12.5 gm. per cent. White blood count was 14,300, with 92 per cent polys; urinalysis, acid; specific gravity, 1.006; proteinuria, 3 plus; microscopic, 40 to 50 red cells, 14 to 15 white cells per high power field. The usual conservative measures employed in the management of anuria—i.e., careful fluid and electrolyte balance, prophylactic antibiotics and forced feeding of a sodium, potassium and protein-free high caloric diet—were instituted. On March 1, hemodialysis (MN-8) was performed for six hours. Blood chemical changes were as

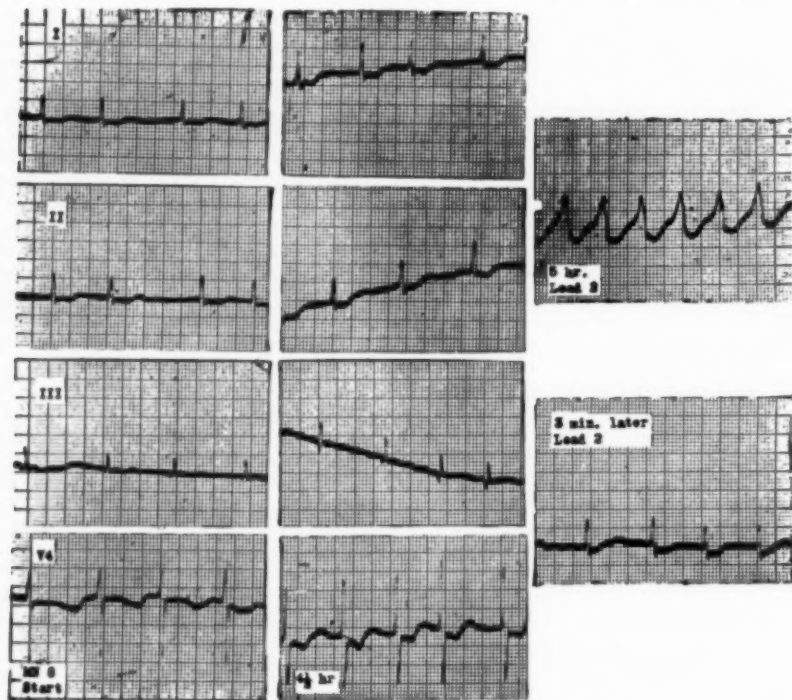


FIG. 2. Electrocardiographic changes during dialysis MN-8, showing increasing digitalis effect leading to ventricular tachycardia which spontaneously reverted.

follows: sodium, 132 to 140 mEq./L.; potassium, 4.5 to 4.1 mEq./L.; calcium, 3.9 to 4.9 mEq./L.; bicarbonate, 10.0 to 14.0 mEq./L.; chloride, 105 to 108 mEq./L.; nonprotein nitrogen, 204 to 92 mg. per cent; creatinine, 10.8 to 6.5 mg. per cent. The patient had been receiving 2 ml. of Digalen daily, and although she had passed practically no urine since admission, no sign of digitalis intoxication was observed. During dialysis, however, the cardiogram which had showed auricular fibrillation and slight ST depression and T wave inversion in leads from the left side of the heart, interpreted as digitalis effect and left heart strain, underwent markedly increased depression of ST<sub>I</sub>, aVL, aVF, V<sub>1</sub>, elevation of STaVR, and merging of T waves into the ST segment until ventricular tachycardia ensued, as shown in figure 2. This

subsided spontaneously in about three minutes. Because of this episode, however, dialysis was stopped, digitalis was omitted and Pronestyl given for four days. Then digitalis was cautiously resumed.

Hemodialysis (MN-10) was again carried out on March 7 for six and one-half hours. Blood chemical changes were as follows: sodium, 126 to 134 mEq./L.; potassium, 4.6 to 4.0 mEq./L.; calcium, 2.8 to 4.2 mEq./L.; bicarbonate, 11.0 to 13.0 mEq./L.; chloride, 81 to 101 mEq./L.; nonprotein nitrogen, 252 to 91 mg. per cent; creatinine, 4.4 to 5.0 mg. per cent. The cardiogram again showed depression of ST<sub>1</sub>, aVF, and V<sub>4</sub>, with T waves lower and more diphasic, but no arrhythmia was observed. From March 1 to March 11 the urine volume varied between 300 and 800 c.c. and then remained over 1 L. *Escherichia coli* sensitive to chloramphenicol was cultured from the blood and urine. Chloramphenicol was administered by mouth but was poorly tolerated, so that blood levels were low. Although nonprotein nitrogen and creatinine did not increase after March 10, the patient slowly lost ground and died on April 8. Autopsy disclosed chronic inactive rheumatic mitral stenosis with superimposed subacute bacterial endocarditis; multiple, septic infarcts of the kidney with extensive destruction of cortical tissue; and chronic peptic ulcers of the duodenum.

Case 6. V. L., a 44 year old housewife, entered March 1, 1952, because of uremia. For several years this patient had been mildly uremic, with blood pressure of 240/120 mm. of Hg and symptoms of asthenia, headache and dizziness. During the two weeks just before admission she became much worse, with increasing anemia, uremia and vaginal bleeding. On entry she was a wasted, dehydrated, chronically and severely ill middle-aged woman with a yellowish, wrinkled skin. Vital signs were normal and the blood pressure was now 130/70 mm. of Hg. The only other noteworthy physical findings were a 3 plus hypertensive retinopathy and a soft irregularity of a portion of the lip of the cervix. The hematocrit was 20 per cent; the white cell count and differential count were not abnormal. Urine was acid; specific gravity, 1.003; protein, trace; microscopic, 6 to 8 white blood cells per high power field.

Since it was felt that an acute exacerbation of her nephritis might be present, and that if this could be relieved she might be returned to the marginal compensation maintained for several years previously, hemodialysis (VLC-9) was carried out for six hours on March 4. Elevation of blood pressure to 180/100 mm. of Hg was reduced by Veriloid, 0.60 mg. intravenously. Blood chemical changes were as follows: sodium, 142 to 143 mEq./L.; potassium, 3.7 to 4.0 mEq./L.; calcium, 2.1 to 5.6 mEq./L.; bicarbonate, 10.0 to 15.0 mEq./L.; chloride, 89 to 97 mEq./L.; nonprotein nitrogen, 240 to 99 mg. per cent; creatinine, 20.3 to 9.3 mg. per cent. The cardiogram, interpreted at the start as showing left heart strain, showed only a late prolongation of QT<sub>c</sub> during dialysis.

The patient was clinically improved by dialysis; she was clearer mentally and was able to eat. The urine output began to rise, but although the nonprotein nitrogen was lower, the patient became paranoid, psychotic and a great behavior problem. Because of this turn of events, her family removed her on March 15 to another hospital nearer her home.

Case 7. R. H., a 28 year old Negro woman, entered on March 11, 1952, because of anuria. Two weeks before entering she had had fever, cough and general malaise, and after a few days of this was given sulfathiazole and bicarbonate of soda. Oliguria occurred somewhat later, but she was not hospitalized until March 8. Severe electrolyte derangement was noted on March 11, and the patient was transferred to Albany Hospital.

She was found to be of low intelligence and was vomiting a great deal. Temperature was 99.6° F.; pulse, 100; respirations, 20; blood pressure, 105/65 mm. of

Hg. Many small blebs were seen over the lower limbs, and the abdomen was distended, somewhat tender and tympanitic. Hemoglobin was 11.5 gm. per cent; white count, 17,000, with 93 per cent polymorphonuclear neutrophils. Urinalysis showed acid reaction; specific gravity, 1.003; albumin, 2 plus; microscopic, 50 to 60 red cells and 20 to 25 white cells per high power field. Marked potassium intoxication was evident in the cardiogram, and this was treated by glucose and insulin intravenously at the time of admission, followed by hemodialysis for six hours on March 12. The run was noteworthy only in the rapid improvement in the cardiogram shown in figure 3. No potassium was in the bath for the first hour.

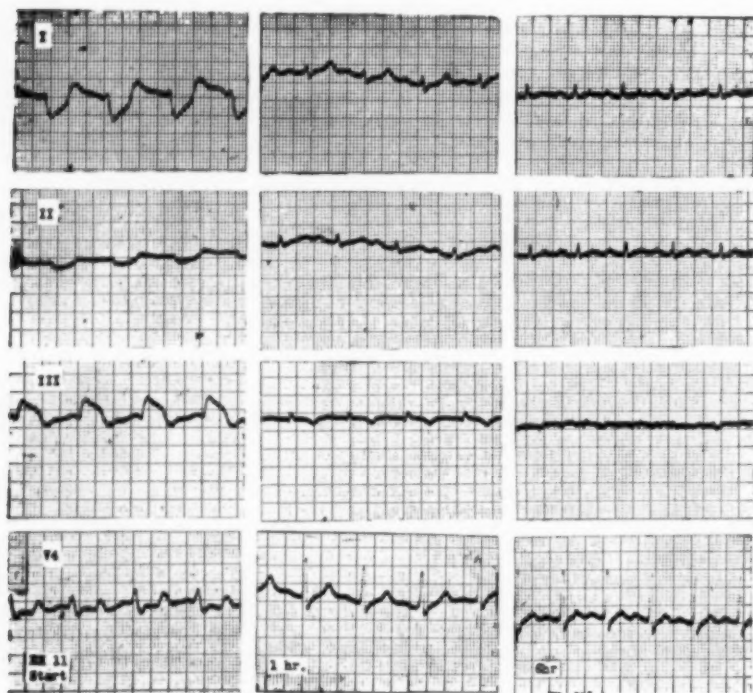


FIG. 3. Electrocardiographic changes during dialysis RH-11, showing correction of potassium intoxication.

Blood chemical changes were as follows: sodium, 117 to 130 mEq./L.; potassium, 8.3 to 4.7 mEq./L.; calcium, 5.8 to 5.3 mEq./L.; bicarbonate, 10 to 13 mEq./L.; chloride, 87 to 94 mEq./L.; nonprotein nitrogen, 156 to 58 mg. per cent; creatinine, 14.9 to 7.7 mg. per cent; sulfonamide, 3.4 to 0.7 mg. per cent. Diuresis began the day after dialysis, and the patient's further course was uneventful.

Case 8. H. R., a 35 year old farmer, entered the hospital on April 21, 1952, because of oliguria. For about six days before entering he did not appear ill, and physical examination was within normal limits, with a blood pressure of 140/82 mm. of Hg. Hemoglobin, white blood cell count and differential count were normal.

The urine was acid; specific gravity, 1.022; protein, 3 plus; microscopic, occasional red cell and white cell per high power field.

Because of the high nonprotein nitrogen and continuous vomiting which ensued, hemodialysis (HR-12) was carried out for four hours. At the end of three and one-half hours, severe epistaxis occurred, and the patient vomited about 300 c.c. of bloody gastric contents. The cardiogram, which had been normal up to the time of hemorrhage, showed lower T waves and ST depression following hematemesis. Vomiting stopped after dialysis, and though the daily urine output remained under 300 c.c. for a week, it then began to rise and the patient made an uneventful recovery.

*Case 9.* H. G., a 40 year old man, entered on April 24, 1952, because of increasing uremia. For about five years the patient had suffered episodes diagnosed as pyelonephritis, and recently he had experienced albuminuria, anemia and blurring of vision. Following a transfusion for his anemia his urine output ceased. His uremia rapidly became worse and he had a number of grand mal convulsions.

He was found at the time of admission to be a chronically ill white man with a pale and puffy face. Temperature and respirations were normal, but pulse was 104 and blood pressure was 150/70 mm. of Hg. Bilateral conjunctival ecchymoses were present. Moist râles were heard diffusely over the posterior lower chest, and the heart was boot-shaped, with a left border of dullness at the midclavicular line, and a Grade II systolic murmur was heard at the apex and aortic and pulmonary areas. The rest of the examination was not noteworthy.

Hemoglobin was 12 gm. per cent; white blood cell count, 11,000, with 87 per cent polymorphonuclear neutrophils. Urinalysis showed acid reaction; specific gravity, 1.010; protein, 3 plus, with 2 or 3 red cells, 10 to 15 white cells and an occasional granular cast per high power field.

Uneventful hemodialysis (HG-13) took place on April 25 for six hours. Frequent premature supraventricular contractions present at the start of dialysis disappeared 30 minutes after the administration of 200 mg. of quinidine gluconate intramuscularly, and T waves which were initially tall and peaked in all leads became lower.

Blood chemical changes were as follows: sodium, 131 to 129 mEq./L.; potassium, 7.6 to 3.5 mEq./L.; calcium, 2.4 to 6.0 mEq./L.; bicarbonate, 5 to 13 mEq./L.; chloride, 72 to 86 mEq./L.; nonprotein nitrogen, 244 to 106 mg. per cent; creatinine, 21.8 to 9 mg. per cent.

The patient responded well to careful dietary management, antibiotic therapy of his urinary tract infection with terramycin, and transfusions of washed red cells. Ultimately a high fluid intake and high urine output were established. He left the hospital, symptom-free, six weeks after entering.

#### DATA

As previously stated, cardiographic change occurred in all but two runs, and in these two instances the lack of change was in itself of interest. Although it was initially suspected that the cardiographic alterations were possibly due to vague toxic effects upon the myocardium, elevation in blood pressure or some undetermined type of stress from hemodialysis, when the group was viewed as a whole it was apparent that each case fitted into a general pattern. All changes were consistent with either correction of a cardiographic abnormality previously attributed to distortion of electrolyte concentrations, or a variation in digitalis effect which might be expected from alterations in electrolyte levels. The cardiographic changes could be

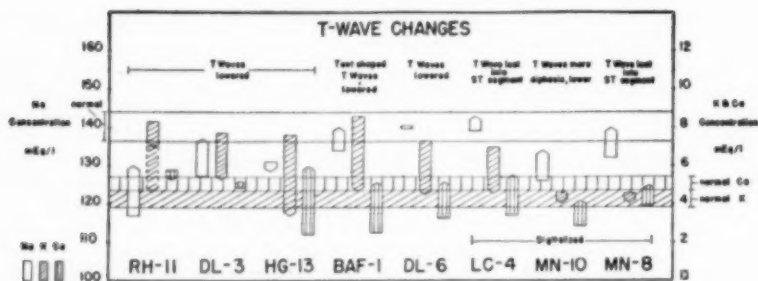


FIG. 4. Analysis of T wave changes. Changes in serum concentrations of sodium, potassium and calcium in each dialysis are represented by the pointed bars, the flat end of the bar representing serum concentration at the beginning of dialysis, and the point of the bar, the final concentration. The potassium bar in RH-11 is divided into two parts, the upper part representing the change during the first hour of dialysis, when no potassium was in the bath, and the remainder reflecting the total six hour change.

summarized in four groups, according to the alterations present: T wave changes, which occurred in eight cases; ST segment changes, in five cases; QT shortening, in two cases; and arrhythmias, in three cases.

Analysis of the T wave changes is presented in figure 4. In cases RH-11, DL-3 and HG-13, T wave changes characteristic of high serum potassium and low serum sodium improved as sodium and potassium concentrations returned toward normal. In cases BAF-1 and DL-6 we observed the phenomenon described by Merrill et al.,<sup>5</sup> in that the original tracings were not so strikingly characteristic of high serum potassium concentrations, since the effect of the high potassium was "damped" by normal serum sodium concentrations, and the change in the electrocardiogram was less marked than in those cases in which sodium was low. In cases LC-4, MN-10 and MN-8, T wave changes were probably due to increasing digitalis effect,

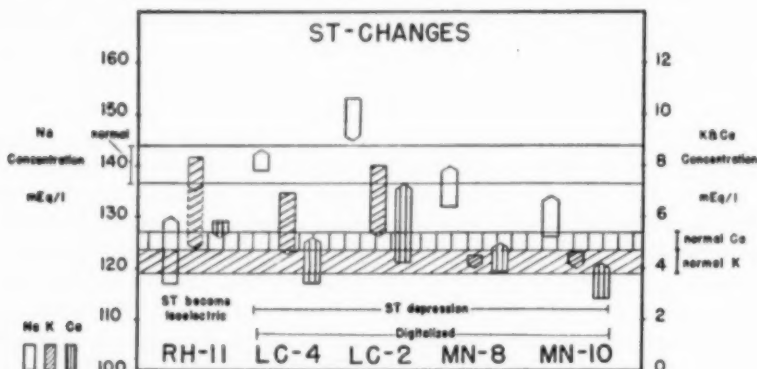


FIG. 5. Analysis of ST segment changes.

associated with increase in body calcium, augmented in case LC-4 by a marked and simultaneous fall in body potassium.

ST changes are shown in figure 5 and fall into two categories. The first, RH-11, represents improvement seen with relief of potassium intoxication. The second category, represented by cases LC-4, LC-2, MN-8 and MN-10, represents increased digitalis effect associated with increase in body calcium in all cases and, in the first two cases, with loss of body potassium also.

The other findings are presented in figure 6. Case VM-7 was the only one with an initially normal cation pattern, and with no cardiographic change exhibited during dialysis. In case VM-5, although rapid correction of a very low serum sodium seemed to cause a marked expansion of the extracellular fluid with a fall in hematocrit and the onset of pulmonary edema, the serum potassium level did not change and there was no change in the cardiogram. The shortened QT interval in case RH-11 was due to the

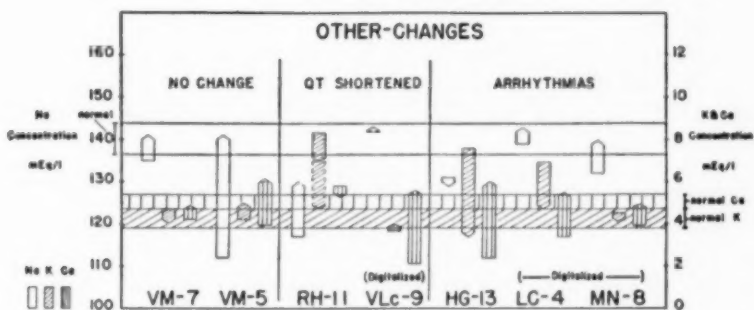


FIG. 6. Analysis of other electrocardiographic changes.

removal of potassium, and the shortening of the QT interval in case VLC-9 could be explained by correction of abnormally prolonged QT time, caused by the low serum calcium at the start.

The production of arrhythmias was possibly the most significant observation. We are unable to account for the runs of premature supraventricular contractions seen in case HG-13. They occurred early in the dialysis and were quickly abolished by parenteral quinidine. But in cases LC-4 (figure 1) and MN-8 (figure 2) the arrhythmias could have been predicted from the increasing digitalis effect, presumably due to the continuing gain in body calcium and loss of body potassium effected by dialysis. Somewhat similar effects have been observed under different circumstances by other investigators.<sup>6,7</sup> The changes seen in case HR-12 were not included in these figures, since ST depression and T wave inversion followed suddenly upon a considerable blood loss from epistaxis, which necessitated stopping dialysis.

In addition, prolongation of the QT<sub>c</sub> was produced after intravenous

Veriloid. This prolongation was due entirely to the bradycardia produced by the drug, with no concomitant change in the actual QT time. This effect disappeared when the rate again speeded up.

#### DISCUSSION

The effects of various cation concentrations upon the electrocardiogram have been well publicized recently. Elevations of potassium concentration lead to an enlargement and broadening and often tenting of the T waves, shortening of the ST segment, widening of QRS and P, and, in higher concentrations, auricular standstill and bizarre appearing ventricular complexes.<sup>5, 8, 9</sup> The inverted T waves of left ventricular strain may be made upright by elevations of serum potassium.<sup>10</sup> Although in general sodium has no effect on the electrocardiogram, the changes due to high potassium are much more marked if associated with a low serum sodium.<sup>5</sup> Hypocalcemia produces a prolongation of the QT time, primarily the ST portion of the QT.<sup>11</sup>

It has been demonstrated repeatedly that altering the concentration of potassium and calcium in digitalized patients may lead to digitalis intoxication.<sup>6, 7, 12-17</sup> Indeed, the former cation is used in therapy of digitalis-induced arrhythmias.<sup>18, 19</sup>

Since 1937, when Cattell and Goodell<sup>20</sup> demonstrated that cardiac glycosides depleted potassium from cardiac muscle, the interrelationship of these two agents has been extensively investigated. All investigators agree that, regardless of the effect of therapeutic doses, toxic doses of digitalis deplete the heart of potassium.<sup>21-28</sup> It has recently been demonstrated that an induced potassium loss, as from diuretics, malnutrition, desoxycorticosterone acetate therapy and intravenous glucose, is capable of producing arrhythmia in digitalized patients.<sup>8</sup> Recovery from diabetic acidosis also may produce an enhanced digitalis toxicity<sup>19</sup> on a similar basis. In the experimental animal, Lown et al. have shown that removing potassium from dogs by dialysis lowers the threshold of digitalis toxicity, while dialyzing them against a high potassium bath raises it.<sup>7</sup> Our cases LC-2 and LC-4 developed an increase in electrocardiographic evidence of digitalis effect concomitant with the lowering of an elevated serum potassium.

In our cases MN-8 and MN-10 an increase in digitalis effect was produced without significant alteration of serum potassium. In these cases, however, there was a definite increase in the serum calcium. Cases LC-2 and LC-4 also had an increase in calcium in addition to the drop in potassium. Many investigators have demonstrated a synergistic action between calcium and digitalis,<sup>13, 15, 16, 29</sup> although Smith, Winkler and Hoff<sup>30</sup> could not produce such an effect in dogs. Baker<sup>12</sup> showed that an increase in potassium concentrations produced more protection against digitalis toxicity than lowering of calcium. The effect of hemodialysis was similar to administering calcium intravenously to a digitalized patient. Although the rise in

calcium was not large, these patients had been receiving normal daily dosages of digitalis at a time when they were anuric.

An alteration of intracellular potassium with no change in serum levels cannot be ruled out as a factor in enhancing the digitalis effect in our patients, although we have no evidence of fluid shift between compartments, in that the hematocrit remained unaltered.

However, Sampson et al.<sup>17</sup> suggest that the serum potassium level is not a reliable measurement of the digitalis protective action, especially if there has been a recent change in potassium balance. They demonstrated that when potassium was used to abolish ectopic beats due to digitalis, the arrhythmia did not return until long after the serum potassium fell below fasting level, and they concluded that some potassium had been fixed in cardiac muscle.

It is not known how the cardiac glycosides themselves are handled by dialysis.

#### CONCLUSIONS

Electrocardiographic changes observed in 11 of 13 consecutive dialyses with a Kolff-type artificial kidney were found to be consistent with the effects of changes in body sodium, potassium and calcium produced by dialysis. In two of the three dialyses showing no cardiographic change, there were no significant changes in serum cation levels, while in the other case transitory cardiographic changes seemed to be associated with blood loss. These cardiographic changes may be favorable, as in instances when serum cation values are returned toward normal. They may, on the other hand, be omens of danger, when serious digitalis intoxication is produced by the gain in body calcium and simultaneous loss of body potassium often produced by hemodialysis. The change in the calcium appears to be equally as important as the potassium alteration in the production of digitalis toxicity.

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## ACUTE TUBULAR NEPHROSIS, A COMPLICATION OF SHOCK\*

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THE acquisition of knowledge concerning this renal disorder merits a summary of recent progress. Ten years ago a report<sup>1</sup> that shock is accompanied by renal deficiency required a mass of supportive evidence. Today those effects are widely recognized and attention is focused upon pathogenesis and conditions of occurrence. For many years isolated observations have been published on azotemia developing after severe trauma, burns and extensive surgery, and during serious infections and intoxications, but the genesis of this disorder was not apparent. This syndrome is not new; it has been described under different names for more than a century, though its relationship to shock has been shown only recently.

### TERMINOLOGY

Beginning with Bright's epochal report (1827), the terms *acute* and *chronic* Bright's disease were applied rather loosely to renal disorders. *Tubal* or *tubular* nephritis soon became synonyms for *acute Bright's disease*, but the latter term remained current for many years. The conditions of occurrence, and the clinical and pathologic features described, indicate that the authors were dealing with the syndrome designated here as *acute tubular nephrosis*. This disorder is always acute and is independent of preëxisting renal disease.

Reinhardt<sup>2</sup> (1852) stated that in *acute Bright's disease* the kidney was large, soft and pale, and the capsule stripped easily. The cortex contained red streaks and flecks; the pyramids were dark and hyperemic. Microscopically, the epithelial cells were swollen and vacuolated and contained granules soluble in dilute acid (a test for parenchymatous degeneration). The tubules contained casts of blood cells, epithelium and pigment which, by obstruction, caused dilatation of the lumina above. Among causes he mentioned cholera, acute exanthemata, typhus, other febrile diseases and *extensive wounds* (*italics mine*).

Cohnheim's<sup>3</sup> (1880) and Ziegler's<sup>4</sup> (1887) descriptions for *acute nephritis* were essentially the same as Reinhardt's. The effects were seen in the tubules, not in the glomeruli. They noted its occurrence after sundry infections, poisoning, toxemia of pregnancy, and febrile, septic and pyemic conditions.

Osler<sup>5</sup> (1892) attributed *acute Bright's disease* to the action of toxic substances upon the kidney. He noted its occurrence from poisons, severe

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infections, malaria, metabolic intoxications and burns. Later he added trauma and extensive surgery to the etiologic conditions. He stated that the urine is suppressed or greatly reduced—4 or 5 ounces per day. It is dark, smoky or reddish brown and contains blood, albumin, casts and debris; the specific gravity is high—1.025 or more. These changes are accompanied by signs of uremia.

Senator <sup>6</sup> (1899) discussed *acute Bright's disease* as synonymous with *acute parenchymatous, epithelial, tubular and desquamative nephritis*. He listed the etiologic factors in two groups: (1) infectious diseases, especially febrile, such as diphtheria, influenza, pneumonia, typhus, typhoid, septicemia, erysipelas, measles, malaria; (2) metabolic intoxications, obstructive jaundice, pregnancy, poisoning as with chloroform, ether, mercury, phenol, tars, etc., and *traumatism*. The pathologic features were like those noted by other authors.

The term *nephrosis* was applied by Mueller <sup>7</sup> (1905) to primarily degenerative renal changes, as distinguished from inflammatory and proliferative disease. Apparently his contribution marks the introduction of that concept and that term.

Adami's <sup>8</sup> description (1909) of *acute parenchymatous nephritis* exemplifies those of this period. The kidneys are enlarged and the cortex is swollen, edematous and pale, in contrast to the deep red medulla. Petechial hemorrhages may be seen in the cortex and in the pelvic lining. The tubular cells are swollen, vacuolated and granular; often they are necrotic or have desquamated from the basement membrane. The lumina contain hyaline, granular or pigmented casts, red cells, and droplets of albumin and debris. Bowman's capsule may contain blood cells and albuminous material. Often it is impossible to draw the line between cloudy swelling and this form of nephritis.

Modern pathologists have added only minor items to Adami's description, as will be noted later. The term *acute parenchymatous nephritis* became the usual designation in English and American literature for this renal disorder.

The treatise *Die Brightsche Nierenkrankheit*, by Volhard and Fahr <sup>9</sup> (1914), led to a new classification of renal diseases. The term *acute parenchymatous nephritis* was displaced without substitution. These authors discussed simple nephrosis but did not identify it with the renal disorder under consideration here. Subsequently, *nephrosis* (*tubular nephritis*) received only transient and fragmentary consideration in treatises on medicine and pathology, although current literature contained frequent case reports on this syndrome. Clinicians often called it *febrile albuminuria*.

The term *extrarenal azotemia* was used by Jeghers and Bakst <sup>10</sup> (1938) and others to denote the absence of preëxisting renal disease. They admit this is a poor term, because renal functional deficiencies cannot be excluded. They attributed the azotemia to combinations of low blood pressure, hypo-

chloremia, dehydration (hemoconcentration), liver damage, protein catabolism and local renal disturbance. They cited the experimental production of oliguria and azotemia by low blood pressure, chloroform poisoning, proteose intoxication, histamine, anaphylaxis, yellow fever, septic infections, sterile abscess and trauma. They reported clinical cases from acute yellow atrophy, coronary thrombosis, arsphenamine reaction, pyloric obstruction, peritonitis, pancreatitis, pneumonia, yellow fever, "hepatorenal syndrome," Weil's disease, shock, transfusion reactions, unexplained vomiting, drug poisoning, allergy, surgical operations and burns. The relationship of many of these cases to shock was recognized.

The urines were characterized by high specific gravity, albumin, casts, blood cells and debris. In some instances, examinations of the kidneys were not recorded; in others, the kidneys were increased in weight, grossly edematous and swollen. The tubular epithelium showed degenerative changes ranging to actual necrosis. Often the lumina contained casts, cells and debris.

Fishberg<sup>11</sup> used the term *prerenal azotemia*, though he admitted there is direct evidence of renal functional impairment. The etiologic importance of peripheral (i.e., not cardiac) circulatory deficiency was emphasized. He recognized shock as a major factor in renal deficiency resulting from the "hepatorenal syndrome," Addisonian crisis, trauma, postoperative collapse, severe infections, burns, coronary thrombosis and other conditions. The renal functional disturbances were attributed to decreased renal blood flow.

The reports of Bywaters<sup>12</sup> and associates on the *crush syndrome* excited widespread interest. Fatal uremia resulting from ischemic necrosis of muscle seemed a unique renal disorder. A later report<sup>13</sup> on 22 cases stated that this syndrome is not peculiar to crush injuries but may occur in such conditions as septic abortion, accidental trauma, blackwater fever (malaria) and transfusion reactions. Yet subsequently Bywaters<sup>14</sup> described this syndrome as "a specific response to a specific type of trauma . . . previously unrecognized." He did not attribute it to shock, descriptions of which were compared "to that other fabulous concept, the unicorn." The clinical features included pallor, low temperature and blood pressure, sweating, thready pulse, decreased blood volume and CO<sub>2</sub> combining power, hemoconcentration, low blood chloride, high potassium, and nitrogen retention. The urine was scanty and dark colored, and contained albumin, pigmented casts, cells and debris. Visceral hyperemia, petechial hemorrhages, edema and parenchymatous degeneration were seen at necropsy examinations. Some readers may recognize certain similarities to shock in the items mentioned. The condition was attributed to "oligemic hypotension." Later, Bywaters<sup>15</sup> decried the view that the renal failure is due to anoxia. He asserted that renal ischemia causes degeneration of the *proximal* tubules, whereas the crush syndrome and mismatched transfusion of blood affect the distal convoluted tubules entirely.

In studies on the pathology of shock, Moon<sup>16</sup> regularly found severe degeneration of the parenchymatous organs. The kidneys showed acute degeneration, ranging to necrosis, affecting all portions of the convoluted tubules; the clinical data in such cases were as described by other observers. In severe cases, this progressed to uremia and death.

Lucké's<sup>17</sup> report on *lower nephron nephrosis* was based upon several hundred cases, including battle wounds, crush injuries, surgical operations, burns, infections, poisoning, transfusion reactions, and shock from other causes. The clinical and urinary findings corroborate those previously described. The kidneys showed the essential features set forth by Adami, with one notable exception: Lucké found the renal damage sharply limited to the distal convoluted tubule and the thick limb of Henle's loop. Other pathologists have failed to corroborate this finding, but the term used by Lucké became popular among internists and surgeons.

Mallory<sup>18</sup> described this disorder as seen in army hospitals near combat areas. Cases of shock from wounds, burns, heat stroke, crush syndrome, anoxia, transfusion reactions and from high altitude aviation were studied. The first effect of shock upon renal function was oliguria, followed by retention of nitrogenous wastes. Regular features were oliguria, azotemia, albumin and pigment in an acid urine. He spoke of this as *hemoglobinuric nephrosis*. Degeneration and necrosis were not limited to the lower nephron.

This sketch of terminology also traces progress toward an understanding of this disorder. Of the numerous terms proposed, only a few are currently used. *Extrarenal uremia* was dropped when the evidence indicated that the functional disturbance is *renal*, though caused by diverse extrarenal conditions. *Nephritis* is not an appropriate term because basically the condition is degenerative rather than inflammatory. *Nephrosis* is historically and morphologically correct. The term *lower nephron nephrosis* is euphonious but appears to be erroneous. Herbut<sup>19</sup> and others have found the degeneration most severe in the *upper* portions of the tubules. Smith<sup>20</sup> observes that all segments of the tubules may be affected, and warns against misleading labels. Bell<sup>21</sup> feels that this term introduced confusion instead of clarification and is a disservice to pathology. *Hemoglobinuric nephrosis* is not objectionable except that hemoglobinuria is not always present. The term *acute tubular nephrosis* describes clearly the most constant and characteristic feature: *acute degeneration of tubular epithelium*.

#### PATHOGENESIS

Renal deficiency has been reported in some 50 diverse conditions, which may be grouped under the following headings:

- Extensive trauma and/or surgery.
- Thermal injuries, including heat stroke.
- Effects of atomic and roentgen radiation.
- Severe infections of diverse kinds.

Abdominal catastrophes, such as perforations, thromboses, peritonitis, pancreatitis, volvulus and others.

Allergic reactions, including transfusions.

Sundry metabolic disorders.

Poisoning with various drugs and chemicals.

Anesthetic agents, barbiturates and others.

Lack of oxygen, from whatever cause.

The only common factors in these conditions are the development of peripheral circulatory failure, often subclinical in degree, and renal tubular damage. The numerous conditions mentioned account for the high occurrence of tubular nephrosis. Several writers have stated that this renal disorder outranks all others as a cause for renal insufficiency and azotemia.

Clinical and experimental studies have yielded results which clarify the genesis of this disorder. Duncan and Blalock<sup>22</sup> devised a clamp by which heavy pressure on the muscles of animals was maintained for hours. Shock developed after this pressure was released. There were hemoconcentration, a decline in the blood pressure, oliguria, dark or bloody urine containing albumin, red cells and casts, and an increase in the creatinine and nonprotein nitrogen of the blood.

Lauson, Bradley and Cournand<sup>23</sup> collected data in 35 cases, including skeletal trauma, hemorrhage, peritonitis, strangulated hernia, burns and head injuries. Shock was recognized clinically in most of these cases. Oliguria was pronounced, and renal clearance tests showed decreased glomerular filtration and plasma flow, roughly paralleling the degree of shock. Their evidence indicated that the renal deficiency results from decreased flow of blood through the kidney, due to constriction of the renal arteries.

Several explanations for the renal complications of shock have been advanced. It was suggested that mechanical obstruction of the tubules caused retention of urine. This explanation is inadequate because only a small percentage of the tubules are obstructed by debris or casts. Also, the size of the kidneys would be greatly increased by this mechanism; actually, the swelling of the kidneys is only slight or moderate.

Some have thought that the glomeruli are unable to function because of decreased blood pressure. However, the blood pressure often had been maintained at adequate levels by therapeutic means, yet renal insufficiency was not prevented. It is known that the glomeruli may be unable to produce filtrate from blood which is abnormally concentrated, but in many instances hemoconcentration had not developed, or it was counteracted by the introduction of fluids.

Some believe that an excess of antidiuretic hormone from the pituitary may be implicated in this syndrome. This hormone will produce oliguria, but such abnormalities as proteinuria, casts, cells and debris would not result from this cause, nor would degeneration and necrosis of epithelium.

Most writers attribute this syndrome to renal anoxia. Years ago

Richards<sup>24</sup> showed that damaged tubular epithelium allowed unselective resorption of the glomerular filtrate into the circulation, hence no urine was formed. Anoxia is a major factor in shock, and of itself causes renal tubular degeneration; hence Richards' explanation seems applicable. Van Slyke,<sup>25</sup> Smith<sup>26</sup> and others endorse the resorption of glomerular filtrate as explaining oliguria incident to shock.

The origin of the renal anoxia is of major interest. Trueta and his associates<sup>26</sup> developed strong evidence that arterial blood may by-pass the cortical areas of the kidneys through expanded glomerular vessels in the juxtamedullary zone. This mechanism was demonstrated in rabbits after tourniquet shock, trauma to the muscles, and stimulation of splanchnic and sciatic nerves. India ink injected into the renal artery was deposited only in the juxtamedullary areas, leaving the outer cortical areas unaffected. This indicated that, under the conditions of their experiments, arterial blood failed to reach most of the cortical tissue. They believe that cortical ischemia thus produced explains the impaired renal function in the "crush syndrome" and in shock from other causes.

This mechanism has been accepted by some and disputed by others. Accordingly, we attempted to repeat some of Trueta's experiments. A rabbit was anesthetized with pentobarbital sodium, and a tourniquet, applied to a hind leg, was released after four hours. Two hours later, hemoconcentration indicated that shock was developing. The left kidney was then exposed and India ink was injected into the renal artery, after which the vessels were clamped; the kidney was then removed and placed in fixative. The right kidney was prepared for determination of alkaline phosphatase.

Microscopic examination revealed that the cortex was diffusely impregnated with deposits of carbon. Contrary to expectation, the juxtamedullary zone did not contain more pigment than the outer cortical area. Repetitions of this experiment gave identical results. In other experiments, shock was induced by narcotizing rabbits deeply with sodium pentobarbital for 48 hours. Injections of India ink caused diffuse deposits in the cortex as in tourniquet shock.

Sections stained for alkaline phosphatase showed no detectable difference between the juxtamedullary zones and the outer cortical zones in either series. In sections stained with hematoxylin-eosin, degeneration was severe in all portions of the convoluted tubules. This was extensive, even after tourniquet shock of only two hours' duration, demonstrating the speed of anoxic effects upon the renal parenchyma. Our findings corroborate those of several other workers.

Van Slyke<sup>25</sup> showed that shock causes an immediate reduction in the renal blood flow. He believed that this is a part of the systemic reaction to a loss of circulating blood volume and that it is due to renal vasoconstriction. If shock is temporary, renal function is resumed; if shock is prolonged, oliguria or anuria may persist, leading to fatal uremia in from

two to 20 days. He does not accept Trueta's phenomena as explaining renal failure due to shock. The shunting mechanism described did not decrease the *total* renal blood flow; it only by-passed the cortex. Van Slyke demonstrated that in shock the *total* renal blood flow was greatly reduced, some times almost to zero.

Sirota<sup>27</sup> reported on renal failure from poisoning with carbon tetrachloride. Clearance tests showed that the renal blood flow was greatly reduced. He attributed the oliguria to tubular damage by anoxia, resulting in unselective reabsorption of the glomerular filtrate. McManus<sup>28</sup> made tests for alkaline phosphatase in the kidneys of subjects dying from renal deficiency after trauma. Disappearance of alkaline phosphatase showed greatest effects in the proximal tubules. He regarded the term "lower nephron nephrosis" as a misnomer for a *diffuse* renal disease.

Maxwell<sup>29</sup> and his co-workers investigated this theory by renal clearance studies in man. Their evidence corroborated that of others indicating a severe reduction of renal blood flow during shock. They showed that the cortical ischemia is diffuse rather than limited to the outer portion of the cortex, as reported by Trueta. These authors found no positive evidence of such diversion in oliguric states resulting from shock of various origins.

Berg, Levinson and Wang<sup>30</sup> produced the syndrome of tubular nephrosis in dogs by intramuscular injections of the toxins of *Clostridium perfringens*. Blood chemical changes and reduced blood pressure characteristic of shock resulted. There was suppression of urine and elevation of the blood urea nitrogen. The urine contained casts, cells, blood and sediment. Microscopic examination showed degenerative changes, most severe in the proximal convoluted tubules. Their studies indicated that the renal effects resulted from disturbed circulation (shock plus anoxia) and perhaps to some degree from the direct effects of the toxin.

Block and associates<sup>31</sup> produced renal deficiency in dogs by experimental hypotension. They maintained the blood pressure continuously at low levels by means of controlled hemorrhages. This procedure resulted in oliguria or anuria, hematuria and albuminuria lasting two or three days after termination of the hypotension. Clearance studies indicated a reduced flow of blood and plasma through the kidneys and a reduction of glomerular filtration. The nonprotein nitrogen rose moderately and the urine had a high specific gravity. Degenerative changes were most severe in the proximal convoluted tubules, but all segments of the tubules were involved. The changes ranged from mild degeneration to diffuse bilateral cortical necrosis. India ink injected into the renal artery indicated that all portions of the cortex were equally affected. There was no evidence of diversion of blood flow from the cortex, as postulated by Trueta. Summarizing the reports of many workers, Smith<sup>30</sup> finds no evidence that this mechanism is operative in man or in dogs. He suggests that the shunting phenomena described in rabbits may not occur in other species.

Any decrease in peripheral circulation brings compensatory reactions into play, including the discharge of adrenalin into the blood. This may cause renal vasoconstriction leading to ischemia, reduced renal function and degeneration. Smith<sup>20</sup> states that during shock the renal blood flow is reduced to very low levels. When shock becomes profound, systemic anoxia develops and affects the renal tissues as well as other organs.

Poisons such as mercury, arsenicals and toxins of infectious or metabolic origins may injure the tubular epithelium directly, with the same results as of anoxia. Probably the combined effects of these mechanisms are responsible for the functional deficiency and the pathologic changes characteristic of acute tubular nephrosis. Mercuric chloride is an example of this group of agents. Early fatalities from mercury poisoning result from shock; later fatalities are due largely to the renal effects of the poison itself.

The management of tubular nephrosis requires thoughtful consideration of its pathogenesis. This is not a primary renal disorder but occurs secondary to some grave condition outside the kidneys. Therapeutic measures will be ineffective unless the primary causative condition can be counteracted or abated. Efforts to increase the renal output are useless because the kidneys are incapacitated; they will not respond to diuretics or to increased fluid intake. The latter will only aggravate the tendency toward edema, always present in peripheral circulatory deficiency.

Attention is directed primarily toward removing the causative agent and toward restoring circulatory efficiency. For example, in shock resulting from intestinal obstruction such as strangulation or volvulus, that condition must first be relieved. Simultaneously the blood volume should be restored and hemoconcentration corrected by transfusions of blood, plasma or other fluids. This must be done guardedly, to avoid edema and cardiac embarrassment from excessive blood volume.

The retention of nitrogenous wastes may be partially relieved by gastrointestinal or peritoneal lavage and by use of the "artificial kidney." Such measures are admirably adapted to the management of renal deficiency due to acute tubular nephrosis. In some instances, patients have been tided over the critical period until regeneration of tubular epithelium occurred and renal function was resumed. The critical period is ended when oliguria gives place to polyuria.

#### SUMMARY

Tubular nephrosis arises from many conditions in which acute circulatory deficiency develops. It is not a primary disease of the kidneys, but is always secondary to grave disorders elsewhere, hence it once was called *extrarenal uremia*.

Clinically it is characterized by oliguria, proteinuria, casts, cells and debris in the urine, and by progressive retention of nitrogenous wastes leading to azotemia.

The outstanding pathologic features are degeneration and necrosis of tubular epithelium not limited to any portion of the nephron.

The pathogenesis of tubular nephrosis includes two major factors: toxins or poisons carried by the blood, and lack of oxygen. The former may be exogenous or endogenous; the latter may result partly from renal vasoconstriction, partly from systemic anoxia incident to shock.

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## ANTIMICROBIAL THERAPY OF PULMONARY TUBERCULOSIS: REVIEW OF SIX YEARS' EXPERIENCE AT FITZSIMONS ARMY HOSPITAL \*

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SIX antimicrobial agents have been subjected to a methodical pattern of clinical investigation since 1946 at Fitzsimons Army Hospital. Approximately 1,300 patients have been evaluated under controlled conditions employing streptomycin, para-aminosalicylic acid, amithiozone, viomycin, terramycin and Isoniazid, either singly or in various combinations.<sup>1</sup> Therapeutic efficacy, bacteriologic cultural and resistance studies, and toxicity formed the principal criteria for evaluating these drug regimens. Summary data on 875 patients observed on the research wards constitute the basis of this report.

Studies were performed on a homogeneous group of patients relative to extent and clinical pathologic type of disease. Almost all were young adult white males with extensive caseous pneumonic and/or cavitary disease. All had moderately or far advanced pulmonary tuberculosis proved by culture prior to initiation of drug therapy. No additional form of therapy except bed-rest was employed during the first 120 days of antimicrobial treatment. Only 7 per cent had received previous drug therapy for pulmonary tuberculosis.

Evaluation has been based on uniform criteria which remained unchanged during the six year span. Roentgenograms of the chest were obtained at monthly intervals and were evaluated by a jury of not less than three physicians. Response was defined as marked, moderate or slight improvement, no change, and worsening. Marked improvement referred to complete or almost complete resolution. Minimal but unequivocal degrees of clearing were graded as slight improvement. Worsening was defined as any extension of the disease in any part of the lung fields, even if other areas were improved. Presence of cavity was evaluated separately and recorded if the outline could be clearly seen on posteroanterior or lordotic films. Sputa or gastric contents were cultured every two weeks on Petragnani's media. All positive cultures were subcultured on Herrold's egg yolk or American Trudeau Society Committee media containing serial dilutions of the drugs that the patient was receiving. If growth on the tube containing 10 micrograms of streptomycin per ml., 10 micrograms of PAS per ml., 10 micro-

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grams of amithiozone per ml., 25 micrograms viomycin per ml., 25 micrograms of terramycin per ml., or 1 microgram of Isoniazid per ml. equaled the growth on the control tube, the organisms were arbitrarily considered resistant to the given antimicrobial agent. All cultures were sensitive to these concentrations prior to institution of drug therapy.

Hemograms were done on all patients at monthly intervals. Audiograms and caloric vestibular function tests were performed every four months on all patients receiving streptomycin and viomycin therapy. Appropriate laboratory tests to evaluate renal and hepatic abnormality or function were performed at monthly intervals on those patients receiving amithiozone, viomycin or Isoniazid.

#### STREPTOMYCIN AND PAS

Streptomycin remains the most effective single drug agent in the treatment of pulmonary tuberculosis, but further evaluation of Isoniazid may challenge this belief. When streptomycin was administered in a dosage of 1 or 2 gm. daily for 120 days to a group of 66 patients, 72 per cent manifested varying degrees of x-ray clearing and 22 per cent showed moderate or marked roentgenographic improvement. Cavities were lost from view in only 5 per cent of the series. Three fourths of the patients yielded sputum positive on culture on completion of therapy, and 76 per cent of the positive cultures were resistant to streptomycin. Slight decrease in hearing and moderate degrees of vestibular damage as measured by serial audiograms and ice water vestibular function tests occurred in 58 per cent of the 66 patients. When streptomycin was administered in dosage of 1 or 2 gm. every third day to 97 patients for 120 days, therapeutic effectiveness equaled the magnitude of that observed in the series of 66 patients treated with daily streptomycin; the incidence of streptomycin-resistant organisms decreased to 33 per cent, and the incidence of eighth cranial nerve damage was only 5 per cent. Spontaneous reversion from resistant to sensitive organisms did not occur within six months in 41 patients treated with daily streptomycin, but was noted in four of 22 patients (18 per cent) who had received intermittent streptomycin therapy.

Eight per cent of 25 patients treated with 12 gm. of para-aminosalicylic acid (PAS) daily for 120 days manifested moderate or marked x-ray clearing, and 33 per cent of those patients positive on completion of therapy yielded organisms resistant to PAS. Cultures from five of six patients resistant to 10 micrograms of PAS per milliliter spontaneously reverted to sensitive within six months following cessation of PAS administration. Gastrointestinal irritability of moderate severity occurred in 4 per cent of the group, but no other untoward side effects were noted. Two patients were not included in this series since PAS was discontinued early in therapy because of drug rash and drug fever.

Whereas PAS did not compare favorably with streptomycin when these drugs were administered singly, the combination produced an additive thera-

peutic effect. A series of 95 patients was treated with 2 gm. of streptomycin every third day and 12 gm. of PAS daily for 120 days. Eighty-nine per cent showed x-ray clearing, and one-half of the group manifested moderate or marked improvement. Two-thirds of the patients were negative by culture on completion of therapy, and none of the positive patients yielded organisms resistant to either streptomycin or PAS. Toxicity (minor changes in eighth cranial nerve function, gastrointestinal irritability, drug rash or fever) occurred in 13 per cent but was of sufficient severity in only four patients to require discontinuance of therapy. The success encountered with intermittent streptomycin therapy suggested combination with intermittent PAS administration. One hundred three patients received 2 gm. of streptomycin every third day and 12 gm. of PAS on the same day for 120 days. Favorable therapeutic results were observed, but 29 per cent of those patients positive on completion of combined drug therapy were found to harbor resistant tubercle bacilli. This approximates the predicted incidence of resistance when intermittent streptomycin is employed alone; therefore, the administration of PAS every third day is not recommended.<sup>2, 3, 4, 5</sup>

D'Esopo advocated the prolonged administration of combined streptomycin-PAS therapy because he noted that drug therapy was often discontinued at 120 days while the patient was still responding to these agents and relapse occurred in a significant percentage of the patients following cessation of antimicrobial treatment.\* An evaluation of 98 patients treated for eight months with 2 gm. of streptomycin every third day and 12 gm. of PAS daily is presented in table 1. Medical collapse measures, predominantly pneumoperitoneum, were employed in 85 per cent of the group after the first four months of drug therapy. Patients requiring major thoracic surgery are not included in this report. Duration of therapy was based on an arbitrary period of two to four months after maximal x-ray clearing was attained. Most patients fulfilled this criterion after a total of eight to 12 months of uninterrupted antimicrobial therapy. Evaluation after 240 days of therapy revealed results superior to those of any previous program of treatment. X-ray improvement was noted in 98 per cent of the patients, and 62 per cent showed moderate or marked clearing. Forty of 70 cavities present prior to drug therapy (59 per cent) were lost from view. Consistently negative cultures were present in 87 per cent of the patients, and only three of 98 patients (3 per cent), or of 13 patients (25 per cent) with positive cultures, harbored known streptomycin-resistant organisms. Roentgenographic or clinical relapse during or in the immediate post-therapy evaluation was a distinct rarity. The true value of prolonged combined drug therapy will require years to assess.

Response to therapy was clearly related to the type of disease and its duration (table 2). Only six of 20 patients (30 per cent) whose disease had existed more than 12 months manifested moderate or marked x-ray improvement after eight months of therapy. In contrast, 72 per cent mod-

TABLE I  
Evaluation of Intermittent Streptomycin-Daily PAS Therapy  
(2 gm. of streptomycin every third day and  
12 gm. of PAS daily)

Interval Evaluated (Days)	120	180	240	300
Number of Patients	98	98	98	46
X-ray Evaluation				
Improved	95	96	96	44
Slight	62	44	34	13
Moderate	32	40	44	24
Marked	1	12	18	7
No change	3	2	2	2
Worsened	0	0	0	0
Cavity lost from view	13 of 70 19%	32 of 70 46%	40 of 70 59%	20 of 38 53%
Bacteriologic Evaluation				
Negative	84	87	94*	39
Positive	14	11	4	7
Resistance studies pending	0	1	1	0
Resistant to 10 mcg. SM/ml.	0	2	1	2
Resistant to 10 mcg. PAS/ml.	0	1	1	1
Resistant to SM-PAS	0	0	1	2
Sensitive to SM-PAS	14	7	9	2

X-ray relapse during therapy: one patient between 180 and 240 days drug therapy.

X-ray relapse post-therapy: two patients 2 mos. following 8 mos. SM-PAS therapy.

\* Bacteriologic relapse: nine of 61 patients observed 4 mos. following 8 mos. of SM-PAS therapy had positive cultures. Thus, positive cultures from 13 patients were available for sensitivity studies.

erate and marked x-ray improvement was noted in the group of 78 patients whose disease was of relatively recent origin.

*Streptomycin Toxicity:* Fifty patients have been evaluated by serial audiograms and ice water vestibular function tests during eight months of intermittent streptomycin therapy (table 3). All received streptomycin sulfate in dosage of 2 gm. every third day for six months, followed by 1 gm. every third day for two months. Evidence of eighth cranial nerve toxicity was

TABLE II  
X-Ray Evaluation of SM-PAS Therapy as Related to Clinical Pathologic Type of Disease  
98 Patients Treated 240 Days

Type of Disease	Improved			No Change	Worsened	Total
	Marked	Moderate	Slight			
I New, Exudative	3	2	0	0	0	5
II New, Caseous Pneumonic	15	36	22	0	0	73
III Old Fibrocasseous	0	0	1	2	0	3
IV Mixed New and Old	0	6	11	0	0	17
Total	18	44	34	2	0	98

TABLE III

X-Ray Evaluation of SM-PAS Therapy as Related to Duration of Disease  
98 Patients Treated 240 Days

Duration of Disease	No. of Pts.	Moderate and Marked X-Ray Improvement	
		No. of Pts.	Per Cent
New Disease (Types I and II); (Less than 6-12 mos. duration)	78	56	72
Old Disease (Types III, IV); (More than 1 year's duration)	20	6	30

observed in 16 patients (32 per cent), but has proved to be predominantly transitory in all following cessation of therapy. Abnormalities appeared most frequently in the higher tones (4096 and 8192 cycles per second) of hearing and in vestibular function. A striking correlation of frequency and severity of ototoxicity with the age of the patient was readily apparent. Seven of eight patients over 50 years of age had some degree of eighth cranial nerve damage; of seven patients who had marked toxicity, five were more than 50 years old. Preëxisting auditory disease also appeared to be a factor in the severity of ototoxicity.

## AMITHIOZONE

Fifty patients received 200 mg. of amithiozone (TB-1) daily for 120 days (table 5). Half of this group were new admissions who had received

TABLE IV

Eighth Cranial Nerve Toxicity of Streptomycin Sulfate  
50 Patients Treated 240 Days

Degree of Damage*	Audiogram		Ice Water Vestibular Test	Total Abnormal Tests	Total Patients
	512-2048 Cycles/sec.	4096-8192 Cycles/sec.			
Slight	3	7	3	13	6
Moderate	1	1	2	4	3
Marked	3	3	5	11	7
Total	7	11	10	28	16

\* Criteria (arbitrary) for evaluation of audiographic and vestibular function tests.

Factor Evaluated	Audiogram	Caloric Vestibular Function Test
No Change	0-10 decibels loss	Nystagmus 90-120 seconds
Slight	11-20 decibels loss	Nystagmus 89-75 seconds
Moderate	21-30 decibels loss	Nystagmus 74-50 seconds
Marked	More than 30 decibels loss	Nystagmus 49 or fewer seconds

no previous drug therapy, while the remainder constituted therapeutic failure during the preceding six to 24 months of hospitalization. Significant gastrointestinal irritability occurred in one-half of the patients, transient hepatic damage in 22 per cent, and mild anemia in 26 per cent. Therapy was discontinued in eight patients prior to the anticipated date of completion because of serious toxicity. Therapeutic efficacy was slight in magnitude as measured by clinical response and serial roentgenograms. When the dose of amithiozone was reduced to 100 mg. daily and combined with 2 gm. of streptomycin every third day in a group of 25 patients, very little toxicity was observed and the therapeutic response was more gratifying. However,

TABLE V  
Amithiozone (TB-1) Employed Singly and Combined with Intermittent Streptomycin (SM)  
120 Day Evaluation of 75 Patients with Moderately and Far Advanced  
Pulmonary Tuberculosis

Regimen	200 Mg. TB-1 Daily	100 Mg. TB-1 Daily 2 Gm. SM Q3D
Number of Patients	50	25
Symptomatic Improvement	Per Cent 52	Per Cent 88
X-Ray Change		
Improved		
All degrees	31	88
Slight	27	56
Moderate and marked	4	32
No change	55	12
Worsened	14	0
Cavity lost from view	0	0
Bacteriology		
Negative	19	48
Positive	81	52
Resistant to 10 mcg. TB-1/ml.*	15	0
Resistant to 10 mcg. SM/ml.*	—	39
Toxicity		
Incidence	78	4
Severity	Moderate to Marked	Slight

\* Percentage based on number of patients with positive cultures on completion of therapy.

39 per cent of the patients whose sputum yielded positive cultures on completion of therapy were found to be resistant to streptomycin. This approximates the predicted incidence of resistance when streptomycin is administered singly every third day.

In summary, it is believed that maximal doses of amithiozone produced definite but slight therapeutic effect and were accompanied by considerable toxicity. Minimal doses failed to delay the emergence of streptomycin-resistant organisms. Amithiozone deserves only a minor rôle, if any, in the family of antituberculous drug agents.<sup>7</sup>

## VIOMYCIN

Early clinical investigation of viomycin revealed significant toxicity with reference to the kidneys, blood electrolyte pattern and eighth cranial nerves when administered in a daily dosage of 30 to 50 mg. per kilogram of body weight. No serious toxicity involving the above systems was encountered in a series of 80 patients when the viomycin was administered in dosage of 2 gm. every third day. Minor toxicity included pain at the site of intramuscular injection, low grade drug fever, skin rash and edema, and renal irritation, manifested by transient albuminuria and cylindruria. When this

TABLE VI

Intermittent Viomycin (VM) Therapy in the Treatment of Pulmonary Tuberculosis  
120 Day Evaluation of 80 Patients with Moderately Advanced or Far Advanced Disease  
Treated with VM Singly or Combined with Streptomycin (SM) Every Third Day  
or Para-aminosalicylic Acid (PAS) Daily

Regimen	2 Gm. VM QD	2 Gm. VM Q3D 1 Gm. SM Q3D	2 Gm. VM Q3D 12 Gm. PAS QD
Number of Patients	22	36	22
	Per Cent	Per Cent	Per Cent
Symptomatic Improvement	76	89	80
X-Ray Change			
Improved			
All degrees	77	83	95
Slight	68	44	76
Moderate and marked	9	39	19
No change	14	14	5
Worsened	9	3	0
Cavity lost from view	6	21	6
Bacteriology			
Negative	36	50	48
Positive	64	50	52
Resistant to 25 mcg. VM/ml.*	7	0	0
Resistant to 10 mcg. SM/ml.*	—	6†	—
Resistant to 10 mcg. PAS/ml.*	—	—	18†
Toxicity			
Incidence	100	100	100
Severity	Slight	Slight	Slight

\* Percentage based on number of patients with positive culture on completion of therapy.

† In all cases, resistance proved to be transient.

drug was employed singly every third day, limited data suggested definite therapeutic effectiveness but considerably less than that noted with streptomycin. Combination with either streptomycin or PAS enhanced the efficacy of viomycin, and favorably modified the expected rate of emergence of organisms resistant to both drugs (table 6).<sup>8,9</sup>

## TERRAMYCIN

Since high concentrations of terramycin are capable of inhibiting growth of tubercle bacilli in vitro, a small group of patients was treated with 7 gm.

of terramycin daily for 120 days. Gastrointestinal irritation occurred in all patients during the first few weeks of therapy but tended to subside or disappear thereafter. The therapeutic effect was encouraging, and this study was followed by a second, of a group of 66 patients treated with 5 gm. of terramycin daily and 2 gm. of streptomycin every third day (table 7). Although profound changes were observed in sputa and fecal flora, no toxicity occurred other than transitory nausea, vomiting and diarrhea. Excellent therapeutic results were noted; they were similar to those experienced with intermittent streptomycin and daily PAS therapy, and no organisms resistant to either streptomycin or terramycin developed. Not included in the evaluation were four patients who did not tolerate all of the terramycin

TABLE VII  
Terramycin (TM) Employed Singly and Combined with Intermittent Streptomycin (SM)  
81 Patients with Moderately Advanced or Far Advanced Pulmonary Tuberculosis  
Treated 120 Days

Regimen	7 Gm. TM QD	5 Gm. TM QD 2 Gm. SM Q3D
Number of Patients	15	66
	Per Cent	Per Cent
X-Ray change		
Improved		
All degrees	80	97
Slight	20	47
Moderate and marked	60	50
No change	20	3
Worsened	0	0
Cavity lost to view	16	11
Bacteriology		
Negative	47	77
Positive	53	23
Resistant to 25 mcg. TM/ml.*	16	0
Resistant to 10 mcg. SM/ml.*	—	0
Toxicity	100	70
Severity	Slight	Slight

\* Per cent resistant based on number of patients with positive sputa by culture on completion of therapy.

because of gastrointestinal irritation; one of these patients subsequently was found to harbor streptomycin-resistant organisms.<sup>10, 11</sup>

Preliminary studies with 2 gm. of terramycin daily combined with intermittent streptomycin have suggested that lower doses of terramycin favorably modify the incidence and emergence of streptomycin-resistant tubercle bacilli.

#### ISONIAZID

One hundred seventy patients have been treated with 150 or 300 mg. of Isoniazid (INH), alone or combined with 2 gm. of streptomycin every third day.<sup>12, 13</sup> Clinical toxicity attributed to INH has been minimal in this

study. Two patients developed drug fever up to 102° F., one patient developed peripheral neuritis, and another had an epileptiform convulsion which necessitated discontinuance of INH therapy. A few patients complained of nervousness and insomnia, which were readily controlled with small doses of phenobarbital. Hyperreflexia occurred in 5 per cent of the group. Other clinical manifestations of untoward drug reactions were absent. Transient disturbance of hepatic function as measured by brom-sulfalein retention and cephalin-cholesterol flocculation tests occurred in 21 per cent of 85 patients treated six months or longer with INH. Drug therapy was not interrupted or modified, and spontaneous return to normal

TABLE VIII

Comparative Data on Streptomycin-Isoniazid and Streptomycin-PAS Therapy  
2 gm. streptomycin every third day combined with 150 or 300 mg. of isoniazid daily (SM-INH) or 12 gm. of para-aminosalicylic acid daily (SM-PAS)

Factor Evaluated	Regimen and Duration of Therapy					
	4 Months		6 Months		8 Months	
	SM-INH	SM-PAS	SM-INH	SM-PAS	SM-INH	SM-PAS
Roentgenographic evaluation						
Number of patients	109	98	97	98	77	98
Moderate and marked improvement	39%	33%	69%	52%	81%	62%
Cavity lost from view	39%	19%	63%	46%	68%	59%
Bacteriologic evaluation						
Number of patients	105	98	93	98	53	98
Negative cultures	89%	84%	94%	91%	94%	96%
Positive cultures	12	14	6	9	3	4
Relapse post therapy	—	—	—	2	—	9
Sensitive	7	14	2	7	0	9
Resistant	5	0	2	3	1	3
Streptomycin	2	0	0	2	0	1
Isoniazid	3	—	2	—	1	—
PAS	—	0	—	1	—	1
SM and INH	0	—	0	—	0	—
SM and PAS	—	0	—	0	—	1
Sensitivity studies pending	0	0	2	1	2	1

values occurred in all individuals. Transient and minor abnormalities of the urine (trace to 1 plus albumin, occasional hyaline or granular casts or rare red blood cells on microscopic examination of the sediment) occurred in the majority of patients treated for six months or more. There was no disturbance in renal function as measured by the blood urea nitrogen or 15 minute phenolsulfonphthalein excretion tests. No toxic effects were observed on the peripheral blood, but transient and low grade eosinophilia was common.

The therapeutic efficacy of INH employed singly was gratifying, and it is believed that this agent possesses approximately the same range of ef-

fectiveness as streptomycin but less than that observed with the combination of streptomycin and PAS. However, 54 per cent of the patients with positive cultures on completion of four months of INH therapy yielded organisms resistant to 1 microgram of Isoniazid per milliliter, and, similarly, 32 per cent were resistant to five micrograms of Isoniazid per milliliter.

The combination of streptomycin and INH in 109 patients produced additive therapeutic effects which equaled or slightly surpassed results obtained with streptomycin-PAS therapy, the drug regimen hitherto regarded as the program of choice in the treatment of tuberculosis (table 8). Only 12 positive cultures were available from 105 patients treated for four months with SM-INH; two were resistant to streptomycin, and three were resistant to 5 micrograms of INH. The remarkably high incidence of cultural negativity beyond four months of SM-INH therapy has made resistance studies difficult to evaluate to date, but all patients continue to show clinical evidence of sensitivity.

#### DISCUSSION

Pulmonary tuberculosis is characteristically a protracted and unpredictable disease which makes clinical evaluation of therapeutic methods difficult and often misleading. Furthermore, it is important to realize that antimicrobial therapy does not deserve all of the credit for the favorable results observed. Control studies are lacking, and investigation designed to evaluate *only* drug therapy would have little practical value today. The data included in this report represent the sum of numerous factors, including inherent host resistance, bed-rest, drug therapy and operative procedures after the acute phase of the disease has subsided. Methods available to evaluate tuberculosis are gross and, therefore, specific comparisons are hazardous. At best, only a few generalizations are permitted.

An attempt has been made to correlate therapeutic results with the many variables a patient may present, such as age, general condition, race, extent of disease, appearance of roentgenographic lesion and trend of the disease prior to drug therapy. In general, a young individual who is otherwise in good health, with disease of recent origin, constitutes the ideal patient for treatment. This type of case predominates in the clinical material studied at Fitzsimons Army Hospital, and accounts for the unusually fine response depicted in these studies. It should be emphasized that the most important single factor in prognosticating therapeutic response to drug therapy appears to be the duration of the disease process prior to the institution of antimicrobial therapy. Drug treatment employed over an adequate period of time is most apt to be definitive in patients with disease of recent origin, whereas it tends to assume a rôle secondary to operative measures or protracted periods of bed-rest in those individuals whose disease has existed for more than one year prior to the institution of specific drug therapy. An exception to this statement is observed in chronic disseminated nodular tuberculosis (nonmiliary hematogenous pulmonary tuberculosis<sup>14</sup>), which

may show a marked response to drug therapy. This was noted in one patient whose disease was known to have been present for nine years.

Therapeutic response is also related to the duration of antimicrobial therapy. In general, the trend of the reversibility of the disease is indicated by the results obtained during the first four to six months of therapy, but such a trend does not suggest the ideal duration of drug therapy. This is usually recognized, in retrospect, after three to six months of x-ray stability and cavity closure, as well as consistently negative cultures. When it is apparent that drug therapy and bed-rest will not achieve these results during the first 12 to 18 months of hospitalization, medical collapse measures or surgical excision and/or collapse should be considered in order to convert the therapeutic plan to a definitive one. The intelligent use of drug therapy today lies in administering combined therapy over a sufficient period of time, appreciating the inherent limitations of antituberculous drug programs, and correlating it with bed-rest and other therapeutic procedures which may be indicated.

Amithiozone, viomycin and terramycin may have a limited application in the therapy of pulmonary tuberculosis, but such cases are the exception rather than the rule. Specifically, it is the policy at Fitzsimons Army Hospital to reserve these drugs for patients who cannot tolerate, or whose organisms are resistant to, at least two of the three major drugs currently in clinical use. They are streptomycin or dihydrostreptomycin, PAS and Isoniazid.

Results obtained with relatively low to moderate doses of Isoniazid, combined with intermittent streptomycin therapy, equaled or slightly surpassed the favorable findings noted with intermittent streptomycin and daily PAS (table 8). Isoniazid is more easily administered than PAS, since fewer tablets are required and gastrointestinal distress is lacking. This is a significant consideration today, when drug therapy is advocated for prolonged periods (eight to 12 months or longer). The combination of 1 or 2 gm. of streptomycin every third day (dose depending on the weight of the patient) with 300 mg. of Isoniazid daily in three divided doses is considered a promising program for the treatment of pulmonary tuberculosis, but adequate studies of bacterial resistance are not available at this time for final evaluation.

The ideal combination of drugs is not known at this time, and perhaps the answer will lie in the concomitant utilization of all three of the major antimicrobial agents available today. Limited experience in the treatment of miliary and meningeal forms of tuberculosis with streptomycin, PAS and Isoniazid indicates considerable promise for this approach.

#### SUMMARY

1. Clinical investigative studies are presented on 875 patients with moderately advanced or far advanced pulmonary tuberculosis treated dur-

ing the past six years at Fitzsimons Army Hospital with streptomycin, para-aminosalicylic acid, amithiozone, viomycin, terramycin or Isoniazid, either alone or in various combinations.

2. Intermittent streptomycin therapy equaled the therapeutic effectiveness observed when streptomycin was administered daily, and was accompanied by decreased drug toxicity and a lower incidence of streptomycin-resistant organisms. The combination of intermittent streptomycin and daily para-aminosalicylic acid is regarded as one of the most effective drug regimens available today. The administration of para-aminosalicylic acid every third day does not protect against the emergence of streptomycin-resistant bacilli.

3. Combined drug therapy proved more effective than any given antimicrobial agent employed singly and, with the exception of amithiozone and streptomycin, was accompanied by a decreased incidence of drug resistance to either antimicrobial agent.

4. Amithiozone was characterized by a relatively high degree of toxicity and a low magnitude of therapeutic effectiveness; this drug deserves little place in the treatment of tuberculosis.

5. Limited studies on viomycin and terramycin revealed definite therapeutic effect, and the combination of either of these agents with streptomycin nearly equaled results obtained with the combination of streptomycin and para-aminosalicylic acid. The high incidence of toxicity, though usually of minor nature, limits the clinical use of viomycin and terramycin.

6. Preliminary studies with Isoniazid are most encouraging, but this drug should not be employed alone because of the high incidence of drug resistance. When combined with streptomycin this disadvantage is minimized, but further experience is necessary with this regimen prior to unqualified recommendation.

7. Drug therapy is most effective against disease of recent origin—less than six to 12 months' duration.

8. Duration of drug treatment is not well defined at present, but it is believed that antimicrobials should be administered for from three to six months following maximal x-ray clearing and cavity closure with consistently negative cultures; thus, most patients with extensive caseous pneumonic disease will require eight to 12 months or longer of continuous drug therapy.

9. Though the results of drug therapy are often dramatic, there is the general realization that it is frequently not definite in a curative sense and must be integrated with an over-all program of bed-rest, as well as medical collapse or surgical measures as the individual case dictates.

#### ACKNOWLEDGMENT

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## SIGNIFICANCE OF THE BUCKLED INNOMINATE ARTERY \*

By EDWARD I. HONIG, M.D., WILLIAM DUBILIER, JR., M.D., and  
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BUCKLING or kinking of the innominate artery implies elongation, tortuosity and dilatation of this vessel. It is usually associated with arteriosclerotic and hypertensive disease of the aorta.

Buckling of the innominate artery may cause right superior mediastinal prominence. This produces roentgenographic findings which simulate aneurysm of the innominate or carotid artery, superior mediastinal tumor, retrosternal thyroid, lymph node enlargement, aneurysm of the aorta, or disease within the apex of the right lung.<sup>1</sup> Recognition of the buckled innominate artery is of clinical significance because its nature is benign, as differentiated from the above lesions. Angiocardiography, by affording an accurate diagnosis through contrast visualization, may eliminate exploratory thoracotomy in such situations.<sup>2</sup>

### NORMAL INNOMINATE ARTERY

The normal innominate artery, including its anatomic characteristics and angiocardiographic appearance, was fully described in a previous paper.<sup>1</sup> It is the largest branch of the arch of the aorta and measures at postmortem studies from 3.7 to 5.0 cm. in length. It arises as the first of the three great brachiocephalic arteries from the ascending portion of the aortic arch. It takes an oblique course upward, backward and to the right, to the level of the right sternoclavicular junction, where it bifurcates to form the right common carotid and subclavian arteries (figure 1).<sup>3, 4</sup>

In the conventional frontal roentgenogram of the chest, the normal right superior mediastinal border is formed by the right innominate vein and the superior vena cava. The normal innominate artery cannot be differentiated from the other mediastinal structures because it does not reach the border. Elongation and dilatation of the innominate artery may result in its forming part of the border, causing a right superior mediastinal prominence.

### BUCKLED INNOMINATE ARTERY

Buckling or kinking of the innominate artery is usually associated with arteriosclerotic and hypertensive disease. Hypertension produces unfolding and dilatation of the aorta, and arteriosclerosis, which usually coexists, pro-

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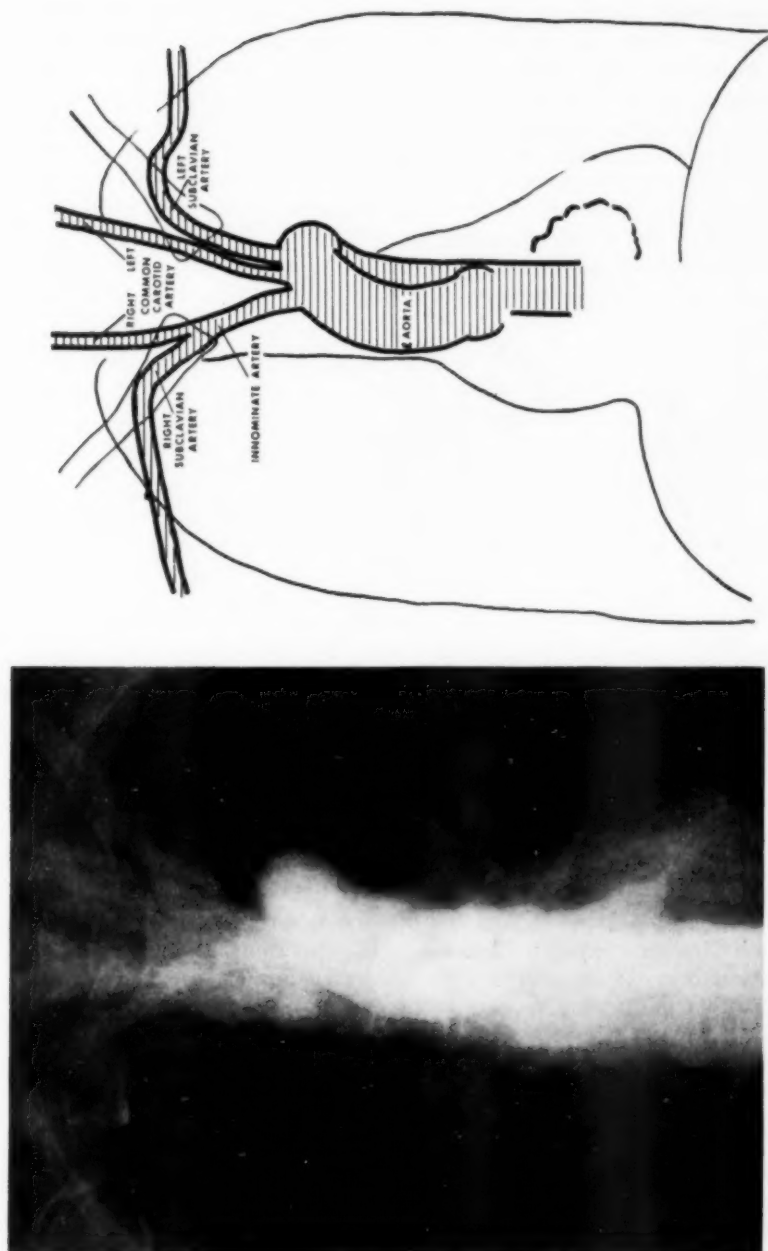


FIG. 1. Angiogram (A) and tracing (B), showing the normal aorta and brachiocephalic vessels. Note the straight course of the innominate artery, which is well within the mediastinal border.

duces concomitant lengthening.<sup>5,6</sup> The aortic arch thus becomes elevated, and tortuosity of the innominate artery and secondarily of the right subclavian artery and right carotid artery may result (figure 2). On the left side the subclavian and carotid arteries are free, and tortuosity is distributed over the length of the vessel without appreciable kinking. On the right side the subclavian tends to anchor the innominate artery at its bifurcation, resulting in buckling when elevation of the aortic arch occurs. The tortuous innominate artery may buckle to the left or right, depending upon the direction of displacement of the origin of the vessel.

Dilatation and tortuosity of the innominate artery and its branches may also occur with syphilitic involvement, usually in association with syphilitic

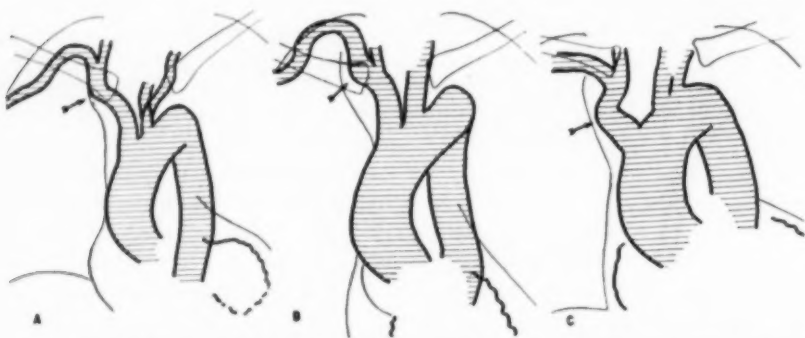


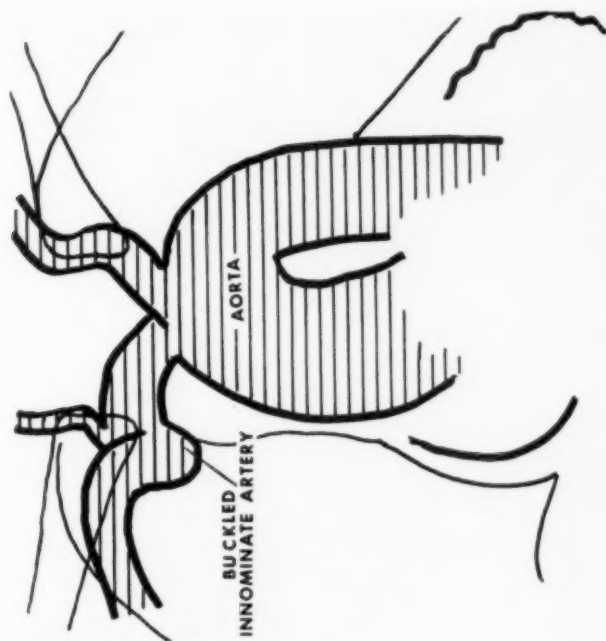
Fig. 2. Tracings of three angiocardiograms (A, B, C), demonstrating unfolding and elongation of the aorta with buckling of the innominate artery (arrows) in patients with hypertension. The conventional chest roentgenograms of each of these patients revealed right mediastinal widening, which was thought to represent tumor or aneurysm.

aortitis. It also frequently accompanies coarctation of the aorta owing to participation of these vessels in the collateral circulation.<sup>3,7,8</sup>

#### CLINICAL FEATURES

A series of 104 angiocardiograms of patients with hypertensive or arteriosclerotic disease revealed 12 instances of significant buckling of the innominate artery. In an additional six cases dilatation and elongation were present, although buckling was not apparent. In many of the angiocardiograms the innominate artery was not adequately visualized, so that the instances of buckling, as well as of dilatation and elongation, are probably more numerous.

The buckled innominate artery may become clinically apparent as a pulsating swelling at the right side of the base of the neck. This may suggest an innominate or carotid artery aneurysm. The swelling may be seen and felt behind the sternal head of the right sternocleidomastoid muscle. It may extend beyond the inner or outer borders or both.



A

B

FIG. 3. Sixty year old woman with hypertension whose chest roentgenogram revealed a right superior mediastinal "mass," thought to be a tumor or aneurysm. The angiocardigram (A) with tracing (B) demonstrates markedly buckled innominate artery. The aorta is dilated and unfolded, owing to hypertension. There is slight tracheal deviation to the right by the aorta.

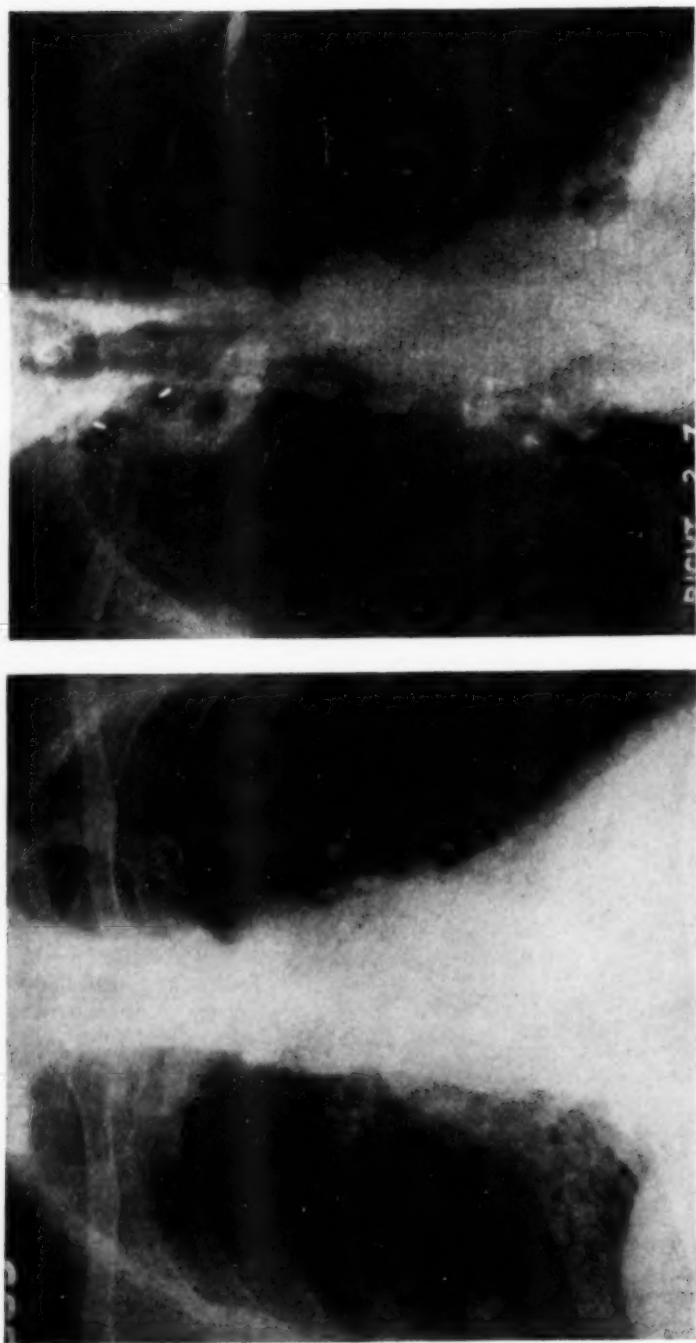


FIG. 4. (A) Conventional frontal chest roentgenogram of a 62 year old woman with hypertension (240/120 mm. of Hg). A right superior mediastinal shadow simulates a tumor or aneurysm. Thoracotomy revealed no tumor; the innominate artery only was found in this region. (B) Postoperative angiogram and tracing (C) of the same patient, which demonstrate that the shadow consists of a buckled innominate and subclavian artery.

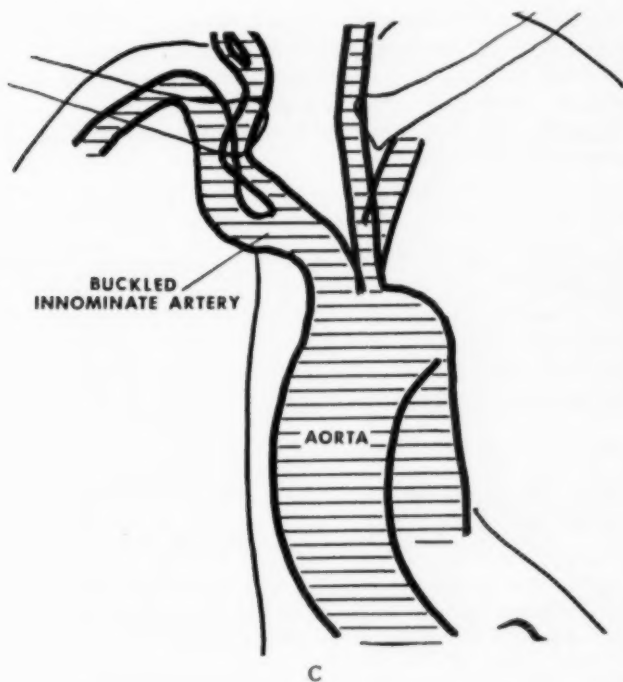


FIG. 4.

Balfour in 1898 reported the case of a woman who noticed a throbbing swelling in her neck. At autopsy the innominate artery was found to be dilated and elongated.<sup>9</sup> Powell in 1909 reported the case of a 78 year old female with a pulsating swelling at the base of the right side of her neck. At autopsy a high division of the innominate with a kinked carotid artery was found.<sup>10</sup> Parkinson studied 48 cases and the relevant literature. He concluded that such palpable pulsations were in most cases due not to aneurysm or localized arterial dilatation, but rather were the result of tortuosity either of the right common carotid or innominate artery, or of both together, with a varying degree of dilatation of those arteries.<sup>6</sup> Of the 12 patients with buckling observed in the present series, eight were female. All had evidence of either hypertensive or arteriosclerotic involvement of the aorta (figure 3). Eight were hypertensive in varying degrees. Four were normotensive. Two had systolic murmurs over the aortic area. One had a to-and-fro murmur at the first intercostal space next to the sternum on the right. Four noted a throbbing sensation at the right side of the neck. In this group palpable and visible pulsations were noted at the base of the right side of the neck. Bruits were heard over three of the pulsating swellings.

One patient had an exploratory thoracotomy when a conventional roentgenogram showed a right superior mediastinal mass (figures 4 A, B). No tumor was noted at operation. Postexploratory angiocardigram confirmed the presence of a buckled innominate artery.

In this series buckling was mistaken for superior mediastinal tumor, aneurysm or retrosternal thyroid.

#### CONCLUSION

Buckling of the innominate artery is of no prognostic significance. Its correct identification and differentiation from other mediastinal conditions will eliminate needless operation. Buckling should be especially looked for in individuals with hypertension and arteriosclerotic heart disease who have right superior mediastinal widening on conventional roentgenograms. Angiocardigraphy will establish the diagnosis in such cases.

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## PRINCIPLES OF PSYCHOTHERAPY IN GENERAL PRACTICE \*

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At the beginning of this century psychiatry was static. Its chief problem was classification of mental disorders from the viewpoint of clinical manifestations, course and prognosis of the disease, and anatomic changes of the brain. Not all cases fitted into the constructed pigeon-holes. This is of course true for any system of human diseases at large. Kraepelin's system is not outdated, as many believe; it still offers the best protection of both the sick individual and society. The potential danger threatening society, and inherent in such disease entities as paranoia, schizophrenia, psychomotor epilepsy, or many varieties of psychopathic personalities, can be met only by a correct clinical diagnosis, that is, by the application of the old-fashioned static pigeon-hole psychiatry. There is no substitute for it, either by psychologic projective tests or by so-called dynamic psychiatry.

Dynamic psychiatry started with Freud, who opened the gate to the wide field of the human mind with all its intricacies. He discovered mechanisms of mental processes, and inaugurated a new psychology, both normal and abnormal, and showed the way and method for its study. As Galdston<sup>1</sup> said in a brilliant lecture, Freud "shook the world"; his advent was one of the great historic experiences, like that of Leeuwenhoek, who uncovered the world of the infinitely small and shaped the tools for its exploration. Psychology is unthinkable today without consideration of the unconscious, of the mechanisms of repression and the disguised emergence of the repressed, of symbolic "organ-language," the mechanism of dreams and of everyday mischance, and of many other discoveries.

It is only fair to recall that it was another Viennese scholar, Josef Breuer, who actually sowed the seeds from which grew psychoanalysis, and who first coined the terms "catharsis" and "conversion hysteria," in the classic of Breuer and Freud, *Studies on Hysteria*, in 1895. It is not without significance that the first light in the elucidation of hidden psychologic mechanisms in sick persons was shed by an internist (not a psychiatrist), whose name became immortal by discoveries in quite different fields (Hering-Breuer reflex regulating respiration; Breuer's investigations on the function of the labyrinthine canals in the internal ear). It is also fair to point out that Freud's method of investigating the mind is open to criticism and is by no means infallible, although there is no better way so far. Unfortunately, this way is not "closed to the public," and it has been used only

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too frequently by persons lacking the proper scientific training and critique. They are chiefly responsible for the enormous antagonism evoked by the psychoanalytic school. If it is true that "many physicians regard Freud's ideas as an ingenious system of nonsense," they must be held to account.

Freud made psychology available as a method to study and reveal the pathogenetic mechanisms of distorted minds. Quite naturally the study centered on the far more frequent cases of psychoneuroses, rather than on psychoses. Those who had not lost contact with reality and society, that is, patients with psychoneuroses as contrasted with psychoses, offered a much more fertile field for psychologic investigations. The violent opposition to Freudian psychoanalysis arose from various sources. Most frequently it was intellectual and emotional rejection of many unproved psychoanalytic statements and fantastic exaggerations, and sometimes it was mental inertia.

In a recent paper<sup>2</sup> on the clinical aspects of hysteria (from Tufts College Medical School and Harvard Medical School), the authors not only reject psychoanalysis but even deny psychology its legitimate rôle in elucidating the mechanism of psychoneurotic symptoms. They believe that the cause of hysteria and the specific mechanisms of its symptoms "will be discovered by scientific investigation, rather than by the use of nonscientific methods, such as pure discussion, speculation, further reasoning from the dictums of 'authorities' or 'schools of psychology' . . . and that fundamental investigation must rest on a firm clinical basis."

Without further discussion of the mutual relations between body and mind, we agree with the current view acceptable to and shared by anyone who does not renounce thinking beyond certain ecclesiastical concepts. Body and mind are the same thing viewed from different angles. Manifestations of human beings may become apparent as somatic or psychic manifestations. The term "psychoneurosis" indicates that they show as psychic manifestations. Hence they must be studied and diagnosed with scientific methods made available by psychology, the science concerned with the psychic aspect of human life. It is preposterous to deny psychology the rank of a science.

While psychology is a science, psychotherapy is an art that has been practiced, consciously or unconsciously, as long as human beings have been harassed by pains and aches. Not so long ago, menopausal syndromes were cured with ovarian tablets whose content of estrogenic substance was practically nil. This is only one arbitrary example of "unconscious" psychotherapy applied by men of science. It is hardly necessary to mention the therapeutic results of magicians, quacks and cultists of different brands. Modern medical psychotherapy is an art based on the scientific background of psychology. Today its necessity is unquestioned, though its indications are not yet so generally recognized by the medical profession as they should be. It is not within the scope of this paper to elaborate on these indications, or to speak about the diagnosis of psychoneuroses and the psychoneurotic

overlay in somatic diseases. Those who are interested might be referred to another discussion of this very important part of medical diagnosis.<sup>4</sup>

One point only might be stressed: The diagnosis of neurosis or psychoneurosis must never be made solely by exclusion, that is solely on the grounds of the absence of signs of an organic disease. Such a diagnosis is justified only if, in addition, positive findings disclose a highly nervous, emotional personality facing a conflicting situation with which he cannot cope. As a matter of fact, this might also happen to persons with any organic ailment, and experience and sagacity are often needed to disentangle this common clinical picture of a mixed somatic and psychic disorder. One should keep in mind that any somatic disease, particularly one of the subchronic or chronic type, involves a potential conflict situation of its own. How such a situation is accepted by its victim, how the physically sick patient solves his problem of adjustment, varies widely according to the individual constitution. The patient as a whole psychosomatic unit requires help.

The internist who relies only on somatic findings and laboratory tests might excel before the pathologist as judge in the autopsy room but he would fail, at least partially, before a higher court judging a physician's activities and goal: to help the sick.

How, then, should the practicing physician apply his psychotherapy? Back-slapping and expressions like "don't worry" or "take it easy" are not enough. The success of "reassurance," a vague term at best, depends on the relation between the doctor's intellectual and moral capacity and that of the patient. In other words, it depends on the doctor's authority. It is not always the doctor who possesses the greater authority.

To apply the proper type of psychotherapy to each individual case of psychoneurosis requires knowledge of the basic principles of the etiology and pathogenesis of these diseases.

There are three factors to be considered in the etiology of psychoneuroses<sup>5</sup>:

1. The constitutional (genetic, hereditary) set-up of a person.
2. Early experiences in life, repressed and coming to the fore in disguised form.
3. Actual difficulties and conflicts which the patient is unable to solve.

As to the first factor, it is unfortunate that it should be necessary today to emphasize the importance of the individual constitution and heredity in the etiology of mental aberrations. There is a host of old and new investigations, as well as daily experiences, conclusively demonstrating this fact, of which Freud himself was well aware. So are "psychiatrists, if they have been well educated, if they have not forgotten their education, and if they retain the scientific attitude."<sup>6</sup> However, we find on page 3 of Levine's *Psychotherapy in Medical Practice* the following statement: "The first of the popular misconceptions is that heredity is the chief cause of psychiatric

disorders. Such a misconception is limiting and stultifying. It produces in the mind of the physician a feeling of hopelessness about personality problems, a feeling that nothing can be done except through some far-off system of eugenics. In the mind of the patient who has a psychiatric disorder, this misconception leads to a feeling of pessimism and hopelessness. It often results in a neglect of those things which can be done. Further, the idea of the primacy of heredity is a most destructive concept in an individual whose family is not free of psychiatric disorders and itself may lead to severe anxiety and to psychiatric symptoms."

Can the success of psychotherapy depend on whether one admits or denies the hereditary factor? It depends on the facts, not on the opinion of the psychotherapist. Freud himself acknowledged the limitations of psychoanalysis in neuroses due to the constitutional factor when he recognized that "neurosis hardly ever develops unless there are constitutional or congenital factors increasing the possibility for such a condition."

Neuropathic or psychoneuropathic constitution is not a disease but a genetic set-up characterized by abnormal excitability and reactivity of the nervous system. Any situation, no matter how common, may become overrated in its affective charge and release inadequate emotions. Occurrences of daily life may arouse abnormal emotional reactions in psychoneuropathic persons. I spoke of "psychic dysmetria" to designate the misjudgment of the affective charge of an experience.<sup>4b</sup> Psychic dysmetria is recognizable by the emotional instability, the excessive, inadequate and untimely reactions of a person and, therefore, his maladjustment to various life situations. Neuropathic constitution is thus only the predisposition to a psychoneurosis, not the neurosis itself. It is likewise the predisposition to various functional disorders that are not psychogenic at all, at least at the outset. This is particularly true if the autonomic nervous system is the chief site of constitutional hyperirritability. Many cardiac, vasomotor or gastrointestinal functional disorders belong in this category.

The belief that psychoneuroses, because they arise from the background of a psychoneurotic constitution, are unfit for psychotherapy is erroneous. The actual disease is accessible to psychotherapy, although the constitutional predisposition persists. The psychoneurotic constitution can hardly be influenced, and it may or may not lead to a new outbreak of an actual disease. Psychoanalysis as a method of treatment pretending to change the constitutionally susceptible personality will fail; aiming only at removal of the actual psychoneurotic manifestations, orthodox psychoanalysis usually is inappropriate and can be replaced by less expensive and less time-consuming and more effective methods of psychotherapy. This will be evident from the following discussion.

Repression of early experiences in life, which come to the fore in disguised form, is the chief principle on which modern psychoanalysts build their conception and treatment of psychoneuroses. Yet repression itself

is nothing abnormal; in normal persons it leaves no traces. Who would contend that he never experienced a feeling of guilt, aggressiveness, rage or hostility toward a member of his family, a friend or superior, that he never felt disappointed in his competitive striving or in his desire to be loved, that he never had a feeling of inferiority, never had to forget some sexual experience of his childhood or adolescence? Yet to dig out such emotions from the subconscious is the aim of psychoanalysis. These emotions serve as guides for a more or less correct interpretation of a personality and should pave the way for its correction. Why should these common emotions and socially unacceptable attitudes, repressed as they were, cause psychoneuroses in only a relatively small group of persons if they prove to have been innocuous for the majority? They cannot be the real cause; they may at best be contributory factors in the etiology of psychoneuroses and formative elements of their shape. These considerations lead back to the conception of individual predisposition, that is, of psychoneurotic constitution which alone makes the pathogenetic rôle of repression understandable and acceptable.

The situation being as it is, it seems hardly worth while routinely to track down all repressed emotional experiences of early life. Even experienced leaders of the psychoanalytic school<sup>7</sup> question the curative value of infantile memories and concentrate on the analysis of the actual conflictual situation. The patient suffers from his incapacity to deal with his actual problems, not from infantile memories. Past events, though intimidating or demoralizing, might have led to the development of the present conflict, but their recollection would hardly aid in solving the actual problem.

The actual difficulties and conflict situations which the patient is unable to solve are the last main and indisputable etiologic factor of psychoneuroses. This is amenable to treatment. The success of the treatment will depend, among other factors, upon the relative importance of the constitutional set-up in the etiology of the disturbance. The more this factor prevails, the less will be the therapeutic result. How, then, should the internist or general practitioner practice psychotherapy?

M. Levine's treatise on *Psychotherapy in Medical Practice* was praised by its publisher for describing 25 methods which all practicing physicians can use, five more advanced methods, and then 10 methods which should be used only by a psychiatrist. Hence there is plenty from which to choose. More important, however, in my opinion, is knowledge of the principles of how a therapeutic result might be achieved. The special technic must be adapted to the individual case, and the choice of the most appropriate method is an art that requires, on the part of the physician, knowledge of human nature, experience and a sympathetic but authoritative personality. The physician must know how to gain the full confidence of the patient and how to overcome the patient's subconscious wish to remain "sick."

For deeply religious patients, recourse to God is often more efficient

than any other method of psychotherapy, and the priest may be more successful than the doctor.

Is psychoanalysis as a method of treatment suitable for eliminating actual conflicts and difficulties? Psychoanalysts claim to achieve more than that. They claim not only to rid the patient of symptoms, but they also attempt a reconstruction of the patient's character, of the personality that led him to the present conflict situation because of his inability to adjust. Character and personality are the result of heritage, plus the environmental factors to which the person has been exposed since infancy. The goal of psychoanalysis is grand, but it lies far ahead, and the way for its achievement is time-consuming and expensive. Can it be achieved at all? Many experienced psychoanalytic authorities, such as Horney,<sup>7a</sup> Oberndorf,<sup>7b</sup> Haldane<sup>7c</sup> and others, express serious doubts. Statistics are not available, and I personally have still to see a psychoanalyzed person who has lost his susceptibility to recurrent neurotic manifestations.

Psychoanalysis is no method for the internist in any case. Its worthy aim does not justify its application in the many cases that can be helped by using a simpler, shorter and more effective technic. The psychotherapeutic technic to be discussed in the following paragraphs is more modest in its goal; it does not claim to change and improve the character of the patient but is often of invaluable help in "curing" the present psychoneurosis. Whether future episodes of psychoneurosis will or will not occur depends on the patient's psychoneurotic constitution and his environmental situation. Constitution will remain, all statements to the contrary notwithstanding.

The principle of this type of "minor psychotherapy" is as follows: Find the actual conflict situation of the patient by taking a thorough and careful history and by asking pertinent questions as to the suspected type of conflict. It is obvious that such a history must be taken sympathetically by yourself, and that to suspect the type of conflict depends on your common sense and knowledge of human nature. Such situations fall into more or less typical patterns. You will suspect one pattern if you have to deal with a young girl (frustration in a love affair), another in dealing with a middle-aged housewife (unfaithful or alcoholic husband, extramarital relations), with a childless or climacteric woman, or with a man or woman living with a mother-in-law. Those are only a few of the more common patterns of conflict situations. To discover the actual difficulties of the patient and to understand the relation of these difficulties to his symptoms require at least some knowledge of what psychoanalysis has taught us about the conversion mechanism and symbolic organ-language. In searching for the actual conflict you also learn plenty about the patient's past and his character.

It is obvious that this procedure requires "activity" on the part of the therapist, which is in contrast to the passivity of the orthodox psychoanalyst, who meticulously avoids any interference with the flow of free associations of his patient. It is in contrast to what has been termed "non-directive

psychotherapy." \* Such a "Monroe Doctrine of the mind," as I venture to call it, "demands no superhuman wisdom or unusual personality from the therapist" \*; indeed, it demands only a listener, whoever he may be, if it is the patient who should find the solution of his problem himself.

It is not always easy to gain sufficient insight into the patient's conflict situation and the mechanism of its action upon the patient's mind and body. The first step of minor psychotherapy is, therefore, to gain this insight. The second step is to convey this insight to the patient, to explain the whole situation as you see it to the patient. He must be told that there is no such thing as an imaginary symptom. The symptoms are always real, only the cause of the symptoms may be imaginary. He must be told that deranged emotions may have repercussions in the somatic sphere, and that primarily mental processes may produce secondary somatic symptoms. The patient must be made to understand the relationship between his symptoms and his emotional stress. This requires, to be sure, a certain degree of intelligence in the patient.

The principle of gaining insight and conveying it to the patient is practiced by most psychotherapists. Even psychoanalysts are beginning to depart from rigid orthodoxy and to advocate a more active attitude toward the patient. The more emotional release that accompanies insight, the better. It seems to be more important that the interpretation of the actual situation offered to the patient be faithfully accepted than that it be correct in every detail.

It is necessary that this analytic activity of the psychotherapist be followed or accompanied by an attempt at synthesis. The patient must be aided in finding some program for his future and must be guided in his readjustment to his life situation. This synthetic activity is all-important, to overcome the subconscious resistance of the patient to being cured and to giving up the "secondary gains" derived from his psychoneurosis. Without the prospect of a more satisfactory life, the patient will not readily accept his conflict as the solution for his psychoneurosis, which serves as an excuse for his inability to handle the difficult situation, to make up his mind and to make a decision. To be successful in this part of psychotherapy requires more than knowledge of textbook medicine and psychology—it requires a humane personality and the ability to use one's knowledge of human relations for the benefit of the patient.

Before we illustrate the working of our short-term "minor psychotherapy" by some instructive practical examples, it might be well to say a word about the now fashionable psychotherapy of internal diseases which were selected for some reason or other to be classed as psychosomatic. We have in mind especially peptic ulcer, ulcerative colitis, bronchial asthma, essential (constitutional) hypertension and others. What an abyss between the attempt to cure a genetic "familial autonomic dysfunction" in children by prefrontal lobotomy,<sup>9</sup> and the concept of old Sir William Gowers, who

once said that if every drug in the world were abolished a physician would still be a useful member of society! I am convinced that the scales of psychosomatic medicine are tipped too much toward the psychic side.

It is not new that the autonomic nervous system regulating tonus and contractions of nonstriated muscles and blood vessels as well as glandular secretions is involved in the pathogenesis of many functional and structural diseases. It is also not new that emotions have their repercussions on the autonomic nervous system, and hence exert their influence upon those various ailments. To take this fact into consideration in the management of any disease has been the practice of good physicians for ages. One must reject the claim that the emotional factor is *the* cause of the enumerated diseases. The individual (genetic) constitution as the etiologic background of these diseases may or may not include emotional instability as part of a psychoneurotic constitution. Emotional conflicts, to be sure, are sometimes contributory etiologic and frequently pathogenetic factors, but their importance must not be overrated. The surgeon Illingworth<sup>10</sup> rightly stated that "the ranks of genuine ulcer cases contain no higher proportion of neurotics than does the population at large. Most ulcer patients, indeed, are the reverse of neurotic. They may be anxious and worried, but . . . generally make light of their suffering, and rarely give up work unless the pain is intolerable." "Formal psychiatry," says Illingworth, has no place in treatment of peptic ulcer. "Informal psychiatry" has always been employed by every good practitioner.

Even more weight must be attributed to the investigations of peptic ulcer by two outstanding psychiatrists, Kahn and Freyhan,<sup>11</sup> who came to a similarly skeptical conclusion: "There appears to be an acute need for scientific restraint or the dissemination of psychosomatic news will acquire an air of propaganda rather than established truth."

What has been said about peptic ulcer holds true, *mutatis mutandis*, for other so-called psychosomatic diseases.

It might be well to reconsider seriously the scientific situation encountered in these ailments, and to include the constitutional viewpoint to a greater extent than is customary today. If we acknowledge that body and mind are only aspects of the same thing from different viewpoints, we choose the somatic rather than the mental aspects for the therapeutic approach to these "psychosomatic ailments." As E. B. Strauss<sup>12</sup> expressed it recently in a Croonian lecture in London, it seems "that the whole of medicine (including psychological medicine) is psychosomatic and that it is only a matter of diagnostic or therapeutic convenience what frame of reference (psychic or somatic) that one selects in considering the case of an individual patient."

Diseases with physical manifestations, such as peptic ulcer, ulcerative colitis, bronchial asthma, essential (constitutional) hypertension and the like, that happened to be classed specifically as psychosomatic on somewhat arbitrary grounds, require a therapeutic approach from the somatic side.

This is logical and definitely safer for the patient. If he requires, in addition, more than the usual "informal psychiatry" (because a psychoneurotic overlay—not causation—may come to the fore in some of those patients), only then might the psychiatrist be called on the job to assist the internist.

#### CASE REPORTS

*Case 1.* A 41 year old childless housewife had been suffering for the last six months from various pains and aches, particularly compulsory belching and anorexia, and occasionally spells of shaking and trembling. Her belching forced her husband to sleep in another room. The patient had received various treatments, including treatment for sinus trouble and a hysterectomy performed four weeks earlier. She reported her symptoms smilingly. Hers was a family of nervous people. The present illness had started when it had been decided that her mother-in-law should move from New York to Los Angeles to make her home with the patient. The mother-in-law was said to be "bossy" and very difficult to get along with. Her own daughter, who lived in San Francisco, refused to take her in. The patient was completely cured of all her symptoms within a week after it was decided to rent a separate apartment for her mother-in-law. Anorexia and belching obviously expressed the patient's resentment, and her feeling that she could not "stomach" the idea of living with her mother-in-law.

Six months later the patient was seen because of dizziness and disturbed equilibrium which had begun a few days before. Asked whether she had to make a decision in the near future, the patient expressed amazement at my suspicions, but they were true. After she and her husband made up their minds to sell their laundromat business she was "cured." Dizziness and disturbed equilibrium are symbols suggestive of lack of decision.

A year later I saw the patient again. She had been all right and had worked until five days before. She complained of "shaking all over," of dizziness and of a "funny" feeling in her head. During the second interview she admitted that she did not get along with her foreman, who wanted her to work overtime. Since no one could replace her in this special type of work (making fancy handbags), she took revenge by getting sick. This mechanism of the present psychoneurosis was acknowledged and accepted by the patient, who lost her symptoms immediately.

The history of this patient illustrates (1) the neuropathic constitution as a predisposing factor to several episodes of actual psychoneurosis; (2) the importance of correct diagnosis and the necessity for "minor psychotherapy"; (3) the insight won by an understanding of the "organ-language" of the patient; (4) the efficiency of "minor psychotherapy" in handling the actual neurosis, with no attempt to change the personality of the patient.

*Case 2.* A 52 year old housewife had been suffering from low back pain for the last four years, particularly when lying down and at night. Extraction of all her teeth, hysterectomy for fibroid (two years before), despite persistent amenorrhea for the past four years, and various injections had been of no avail. Physical examination was negative; the mobility of the vertebral column was not impaired; there were no signs of a diseased disc, and no significant abnormalities of the spine on radiograms. The patient had known better times; since her immigration she had had to bear a heavy load, and to stand on her feet as a saleslady. Her back was not strong enough to carry the load, obviously expressed in organ-language. The patient accepted this interpretation at the second office visit and lost her backache.

*Case 3.* A 54 year old English woman accompanied her husband on a business trip to the United States. From the moment of her arrival in New York she lost

her appetite completely, became nauseated at the sight of a dining room, could not swallow solid food, and felt unable to join her husband at dinners given in his honor. The patient had had hematemesis three years before and had been diagnosed as a case of gastric ulcer; however, there had been no symptoms of the ulcer since then.

From the history it was obvious that the patient's anorexia was of psychic origin, whether or not she had a peptic ulcer. I used the "surprise technic," that is, I started immediately with psychotherapy by declaring: "You are a great patriot, and resent the contrast between the food situation in your country and ours. Don't you?" The intelligent but nervous and introverted patient confirmed my assumption. She was advised to take her dinner the same evening alone in her hotel room and was assured that she would be able to enjoy it and to attend all future dinner parties with her husband. This was actually the case, and the physical examination (including fluoroscopy) done five days later revealed no abnormality. The patient felt perfectly well and enjoyed the hospitality of Hollywood.

*Case 4.* A once famous, 34 year old European prima ballerina came to America in 1938 for political reasons and had to make her living as a saleslady. At this time she began to suffer from continuous low back pain, especially on standing and walking. Roentgen-ray studies revealed partial sacralization of the fifth lumbar vertebra; that is, its left transverse process formed one mass with the sacrum. There was a corresponding mild lumbar scoliosis. The patient was treated with massage and with two injections a week for an entire year, and eventually was put in a brace. This relieved her backache, but the prospect of having to wear a brace all her life made her very unhappy. She had been told that an operation would be necessary if she did not want to wear the brace. When I saw the patient in 1942 she could not suppress her tears, and complained bitterly of her fate. Since her vertebral anomaly was congenital and had caused no symptoms for 34 years, and since her backache coincided with a great emotional tension, it was immediately clear that a psychologic rather than a physical factor must have been responsible for the back pain. This was confirmed by the following report:

She had continued to perform every morning the strenuous physical exercise she had been doing since she started her ballet career. I could not help admiring the acrobatic distortions of her body when she demonstrated the type of exercise. The amazing thing was that the patient felt no pain at all when practicing. She admitted that this hour of daily practice was the only happy time of the day. It was obvious that the patient lived in the past during this hour—the unhappy present life was forgotten for a while, and old glories were relived.

A simple explanation of the situation to the patient was sufficient to cure her promptly. The most difficult job was to convince her of the unimportance of the abnormality of her spine. The next day she left the brace at home and had no subsequent pain.

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## THE RELATIONSHIP OF THE HABITS OF THE HOUSE MOUSE AND THE MOUSE MITE (*ALLODERMANYSSUS SANGUINEUS*) TO THE SPREAD OF RICKETTSIALPOX \*

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It was prophetic that one of the early and undoubtedly most widely read reports of Rickettsialpox should have appeared in *The New Yorker* in August, 1947.<sup>1</sup> At the time of the Kew Gardens outbreak in 1946, investigations established *Rickettsia akari* as the etiologic agent of the disease and identified the rôle played by the mite, *Allodermanyssus sanguineus*, and the house mouse in transmitting the disease to man.<sup>2,3,4</sup> Until a small outbreak occurred in an apartment house in Hartford in 1952,<sup>5</sup> only two other naturally occurring cases, both from Boston,<sup>6,7</sup> had been reported beyond the metropolitan limits of New York City. This sharp confinement of the disease to urban districts and its unpredictable appearance in other localities suggested that some explanation for its distribution might be found in a better understanding of the habits of the house mouse and the mouse mite. An early impression that the house mouse was rather addicted to a higher standard of living led to a study of the relationship of the distribution of cases to economic levels in various sections of the city. The results of these investigations suggest explanations for gross variations in the distribution of cases.

The house mouse, with his right to peaceful domicile, enjoys a high degree of human toleration, due largely to his shy qualities of personality, a firm and affectionate place in our folklore, and a certain sympathy on our part for his position in the scheme of things. It is only when mouse- or man-made conditions force him into an unnatural course of more open and aggressive activity, or the destructiveness of mice in masses becomes apparent, that thorough extermination measures are undertaken.

Because mouseproofing of an occupied building is a practical impossibility, all houses harbor mice at various times and in greater or less numbers. Their activities are concerned with feeding, breeding and rearing the young with minimal expenditure of effort, in pursuit of which they show a strong tendency to follow established lines of travel. Peculiar to the mouse are his capacity to get through an aperture one-half inch in diameter, his ability as a climber and jumper, his capacity to survive on a suitable diet

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without water for months, and his remarkable fecundity. Under normal circumstances it can be assumed, on the basis of his enormous capacity for reproduction, that a mouse-infested environment is saturated with mice up to the limits of available food and harborage. Mice can exist under the most variable conditions and extreme ranges of temperature. It has been estimated that few house mice under normal conditions survive longer than one year. The only significant enemy of the mouse in our American urban environment is the formidable Norwegian rat, whose presence and competition diminish the available supply of food. The quantity of food and the conditions under which it is available are the factors that control both the size of the mouse population and the range of its activity.

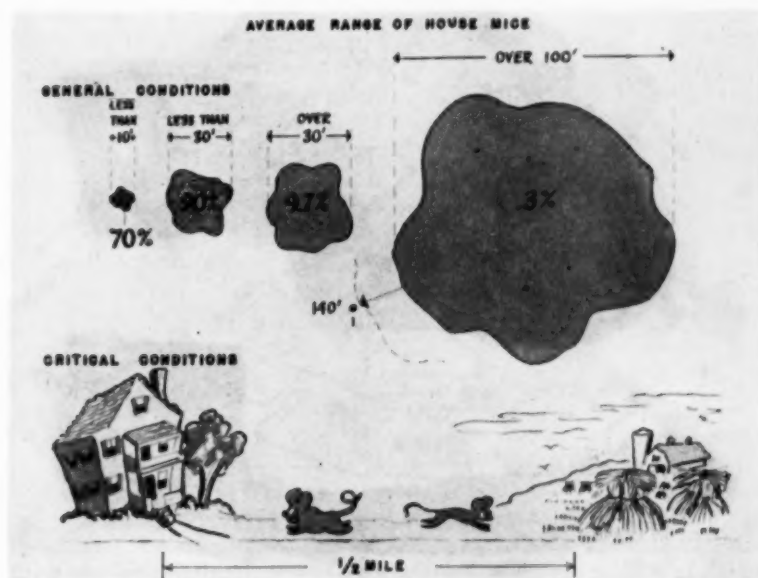


FIG. 1.

Figure 1 represents schematically the range of activity of 1,572 house mice determined by identification and multiple trapping over an eight month period. The experiment was carried out in two frame buildings housing experimental animals where food was generally available.<sup>8</sup> Seventy per cent of the mice did not move out of an area of over 10 feet, and 90 per cent confined their activities to an area of 30 feet. Only six venturesome or possibly maladjusted mice ranged on any occasion during this period over 100 feet. One mouse, the Dr. Livingstone of the group, extended his travels to 140 feet on one expedition, the maximal range recorded. Under

the conditions of this study these observations indicated that the house mouse was essentially a stay-at-home and, except for a small wandering minority, enjoyed a very limited cruising range. Correlated data also suggested an inverse relationship between the amount of shelter available and the cruising range, as well as a greater tendency to venturesomeness on the part of the male compared with the female. Once a mouse settles down and establishes a territory it usually, though not always, remains there for life. Although mice have been observed to live out their respective lives in a single bag of grain, where a sudden shift in the ratio of available

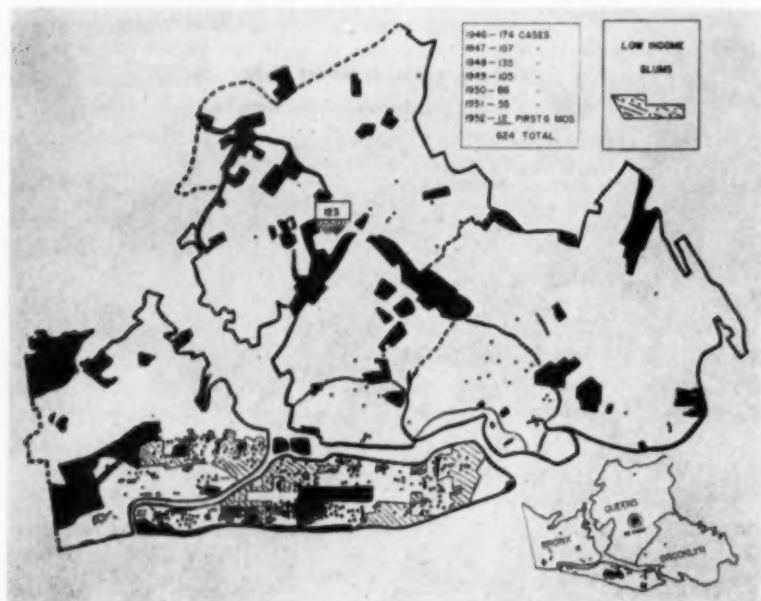


FIG. 2.

food makes conditions for survival critical, ranges of activity of surprising extent have been noted. In one instance nightly excursions of house mice into wheat-seeded fields and their retirement by day to buildings and hedgerows nearly half a mile distant were observed.<sup>9</sup> With these observations in mind we will consider the distribution of cases of Rickettsialpox within the metropolitan area of New York City.

On this map of New York City, excluding Staten Island, are spotted 624 cases of Rickettsialpox reported to the New York City Health Department as of July, 1952. The patches of gray indicate parks. The insert lower right, from Greenberg,<sup>4</sup> illustrates the distribution of cases in 1946

spotted on a somewhat different map covering the same area. The spectacular outbreak in Queens totaling 123 cases is represented on the larger map by the number "123." In 1946 there was a tendency to grouping of cases in lower Manhattan, east and west of Central Park and certain sections of the Bronx.

The occurrence and distribution of cases in Manhattan and the Bronx in the last six years suggest continuing activity and extension of the endemic areas represented by the group of cases in 1946. In addition, a heavy seeding of cases has occurred in the northwest portion of Manhattan Island, and isolated cases have developed in other areas. This flourishing state of affairs in Manhattan and the Bronx stands out in sharp contrast to the relative quiet reigning in Brooklyn and Queens.

In Brooklyn and Queens combined, only 36 cases were reported during the same period, the majority occurring at widely separated points during the same year. In a few locales the juxtaposition of two or three cases occurring either during the same year or over one or two consecutive years suggests that the seeds of an endemic focus were present at these points but the soil was unfavorable for growth and activity. Only at the site of the original outbreak in Kew Gardens, where 26 cases subsequently developed, was there any significant continuity of host infection. All of these cases occurred within the geographic limits of the original outbreak, implying a persistence of those conditions limiting the spread of the infection.

The crucial factor responsible for the striking difference in the behavior of the disease in the Manhattan-Bronx and Brooklyn-Queens sections of the city would not appear to be population density. In the slum areas of Manhattan, where population density is greatest, cases continue for the most part to be relatively scattered, for reasons which will be discussed later. Also the greatest concentration of cases within a limited area, the original Kew Gardens outbreak, developed in a group of modern, well-planned, uncrowded apartment houses surrounded by lawns and gardens.

In addition to differences in population density between the Manhattan-Bronx and Brooklyn-Queens sections, there is a marked dissimilarity in the original planning of dwellings. In the Manhattan-Bronx section of the city, on the one hand, housing construction consists largely of three- to six-story structures plastered side by side along an entire city block, separated only by walls or partitions and boasting at best a small back yard. The Brooklyn-Queens section was originally developed as a suburban area by individuals desiring single family units of one to two stories with front and back gardens and some space between dwellings.

The pressure of increasing population has been felt in both areas and has resulted in cramming the buildings with several times as many people as they were intended to contain. This pressure has been felt to the greatest extent in the Brooklyn-Queens section, in those parts nearest to Manhattan. The areas of Brooklyn and Queens which now, as a result of remodeling and

subsequent construction, have come to reflect more closely the density of housing one finds in Manhattan, are the portions extending west from line "B" to the Navy Yard in Brooklyn, and west from line "Q" to the East River in Queens. Though this latter is principally industrial it does contain small scattered areas of congested housing. The majority of cases of Rickettsialpox in the Brooklyn-Queens sections fall within these areas. Beyond the lines and extending eastward, housing, with the exception of a few large apartments, consists of individual homes built on individual lots.

Although no direct measurements have been made on the ranges of activity of house mice in large blocks of dwellings constructed in a wall-to-wall fashion, certain assumptions appear justified on the basis of what knowledge we have of their habits and such observations of their range of activity in buildings as have already been described. The mice would find access to all units within the block. Within it would be innumerable colonies of mice living in close proximity to available sources of food. The average range of mice in each colony would approximate 12 feet, and contact between colonies would exist at the perimeters, where overlapping of ranges chanced to occur. Contact over greater distances would be maintained by a small minority of rovers and an occasional explorer. Larger shifts in mouse population within the block would be expected to follow marked alterations in the quantity of available food at any point. These conditions would favor the spread of Rickettsialpox, once introduced, throughout the block.

In Brooklyn and Queens, where housing consists predominantly of smaller separated individual units, less continuity in the mouse reservoir would be expected. Only a major disruption in the conditions in a dwelling threatening the survival of the local mouse population would force its activities or migration beyond the confines of the building proper. Except under such extreme conditions, overlapping of ranges should not be expected to occur. Contact with the mouse population at large would be affected under normal conditions only by the extremely venturesome mouse, or by the inadvertent introduction by man of a foreign mouse into the local colony. Such conditions would favor a minimum of spread from any endemic focus. If the disease were endemic at a number of widely separated points, one would expect to find a scattering of cases over a large area. In such an environment, also, the controlling factor of available susceptible hosts might be expected to play a larger part in reducing the activity of the disease and its tendency to persist at any endemic point. These two assumptions appear to find substantiation in the history of both the Kew Gardens and the Hartford outbreaks. In each instance the disease did not spread to dwellings where large, active mouse populations existed under entirely similar conditions. In the case of Hartford the distance between the apartments was approximately 20 yards. Subsidence of both outbreaks can be correlated more closely with a decrease in the population of susceptible

hosts than with the initiation of public health measures directed at controlling the disease. It has been suggested by Greenberg that the recurrence of cases at the Kew Gardens site probably reflects in large part re-introduction of susceptible hosts into the environment.<sup>10</sup>

An apparent tendency to a concentration of cases around parks was noted in some instances. The possibility was considered of the migration of mice from dwellings to adjacent parks during the summer, as well as their invasion of nearby buildings during the fall and winter. Trapping surveys in various parks have shown a quantitatively stable population

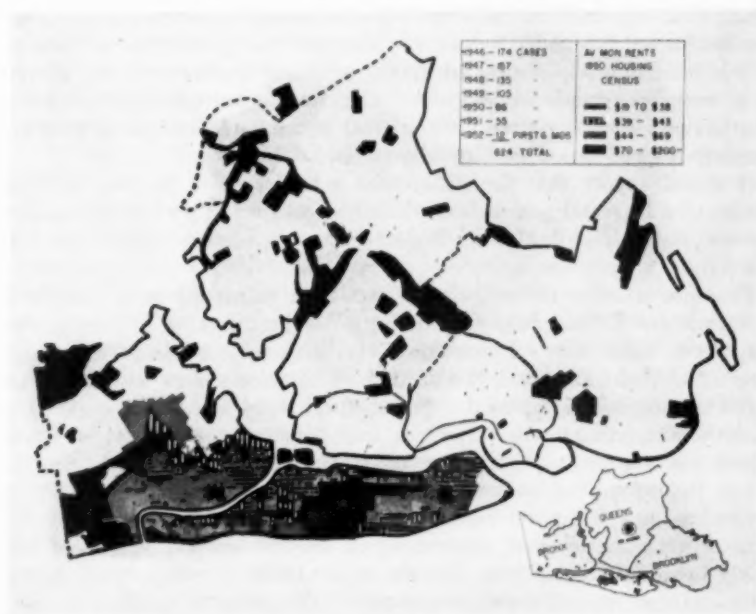


FIG. 3.

throughout the year,<sup>10</sup> suggesting that such migrations, if they occur, are not large. The dissemination of the disease from infected park mice would depend on the capacity of the mite to survive under such conditions.

Data obtained from a survey of rodent ectoparasites in New York City revealed a direct correlation in house mice between the presence of specific antibodies to Rickettsialpox and infestations by *A. sanguineus*. The data were insufficient to indicate whether the disease can flourish in outdoor house mice.<sup>16</sup>

Figure 3 represents the spotting of cases on a similar map of New York City on which is indicated the relative standard of living in various sections

of the city as reflected by ranges of average rent paid in 1950. The relative scattering of cases in the poorer slum sections of Manhattan and the Bronx, when compared with the greater number and concentration of cases in the middle and upper income areas (figure 2), is interesting. That this disease should enjoy a lower level of activity where both wall-to-wall housing and population density are at their peak presents something of a paradox. The solution appears to rest largely in the character and tastes of the Norwegian rat. In these areas, where efforts at sanitation enjoy minimal if any success, this natural enemy of the mouse has settled down happily amidst a profusion of garbage and litter, and established his domain. It is from these sections that over 300 rat bites are reported yearly.<sup>11</sup> Mice exist in these areas but in much smaller numbers. The unfriendly relationship between rats and mice is nicely illustrated by the results of rodent trapping surveys which have been made in and about the dwellings from which cases of Rickettsialpox were reported.<sup>11</sup> In 1,800 premises investigated, rats and mice were trapped in conjunction in only six instances.

It would appear that the differences in the type of housing and the presence of a large rat population in slum areas are factors having a strong influence on the distribution of Rickettsialpox in various sections of New York City.

The mouse mite, *A. sanguineus*, has been recovered in a number of localities in the United States, including Washington, D. C., Tucson, Arizona, New York City, Philadelphia, Indianapolis, Boston, Champaign, Illinois, Salt Lake City and Hartford.<sup>12</sup> This mite shares with other terrestrial arthropods a tracheal type of respiratory apparatus and, being poikilothermic, its growth, activities and survival are intimately related to both the temperature and the relative humidity of its environment. Within the ranges of temperature and humidity necessary for biologic activity, the metabolic and reproductive processes are slower at the lower levels of temperature and accelerated at higher levels. Mites die very quickly in a dry atmosphere. As the upper limits of temperature are approached these processes are accelerated to the point of exhaustion and a decrease in the number of mites occurs. No direct observations have been made on the effect of changes of temperature and humidity on the development and activity of *A. sanguineus*. Harboring *R. akari* does not appear to have an unfavorable effect on the mite. Although not demonstrated directly it is presumed that the larvae of infected adult mites are themselves infected.

Some direct observations have been made on a collection of *A. sanguineus* which were fed on immature white mice and maintained for a short period under experimental conditions.<sup>13</sup> From the larval form it was observed to pass through two nymphal stages before becoming adult. Both nymphs and adults feed on blood. Adult mites tend to feed several times, laying eggs over a considerable period of time after each feeding. They have been

observed to live for six weeks without accepting a blood meal. At Kew Gardens they were found in large numbers on the walls of incinerators in the basements of the apartments and in the vicinity of mouse nests and runs. In the apartments the mites were found on the walls and baseboards in the warm proximity of radiators, as well as on ceiling light fixtures.<sup>14</sup>

*A. sanguineus* is a temporary parasite requiring (under experimental conditions) one to two hours to feed to repletion before leaving the mouse.<sup>13</sup> Parasite counts on individual mice from colonies infested with *A. sanguineus* have shown a range of from one to 10 mites per mouse, with an average of four.<sup>13, 14</sup> At Kew Gardens *A. sanguineus* was found on the walls and ceilings of incinerator rooms 10 to 12 feet distant from where mice were feeding or had their runways. Although apparently perfectly capable of covering considerable distances under their own power, either in search of a blood meal or to find the most suitable environment in the vicinity for growth and survival as temporary parasites, the principal means of dispersion is probably by way of the mice, which scatter these mites wherever they happen to go.<sup>14</sup>

The above observations suggest that housing conditions where relatively low temperatures prevail, or where heating is achieved without consideration of humidity, would be unfavorable to multiplication of *A. sanguineus*. One would expect that such conditions would be found more frequently in slums, and that, in addition to the rôle played by the rats, these might act as a limiting factor on the spread of the disease in these areas. Although the ideal limits of temperature and humidity for the rapid multiplication of the mite have not yet been determined, the basement incinerator and its immediate environment would appear to be favorable for the development of this mite.<sup>4</sup> Again, this method of garbage and trash disposal is, perhaps unfortunately, a feature of the better class of apartment dwellings.

The conditions present at the site of the outbreaks in Kew Gardens and Hartford, which appear to lend themselves to the greatest activity of the disease, deserve consideration. The site of the Hartford outbreak was a fashionable Tudor structure of three stories, consisting of six handsomely furnished, well-kept, seven- to eight-room apartments, housing a total of 13 adults. This building and a companion apartment of similar structure 20 yards distant, also mouse-infested, in which the disease did not occur, were both surrounded by ample, well-kept lawns and gardens. All of the occupants, with the exception of the maids, had been in residence for a minimum of four years and, since occupancy, had been aware that the building was heavily infested with mice. One kindly but predatory elderly widow boasted of having trapped 20 mice in an ordinary snap trap over the course of a single weekend. Because of the infestation of mice, the kitchens were kept scrupulously clean and special care was taken in the storage of food. All the garbage and trash were thrown down the two incinerator chutes. In January, 1952, eight of the 13 occupants fell ill with Rickettsialpox. The

diagnosis was established in four of the cases by the appearance of specific complement fixing antibodies in high titer in samples of sera taken from two to six weeks following the onset of clinical symptoms. In the remaining four cases specific complement fixation reactions were not obtained. Of these cases, two received effective antibiotics and the remaining two ran a very mild clinical course. In one no primary lesion was discovered. The means by which the infection was introduced was not definitely established.

Figure 4 is a schematic drawing of part of the building, illustrating not only the existing conditions but also the carefree attitude the mice had acquired in such a congenial environment. The absence of fire stops in the

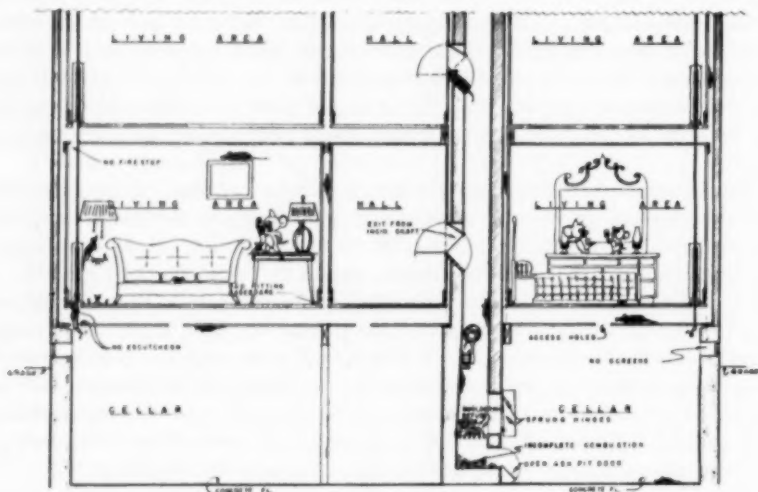


FIG. 4.

walls and escutcheons about pipes, cracks left by slight settling of the floors, and several holes in the basement ceiling near the incinerators allowed the large mouse population free access to all parts of the building. Although no breaks in construction in the walls of the incinerators were visualized, there was good reason to believe that the mice had access to the incinerators at one or more points above the basement. The fact that the incinerators were fired each morning around 7:30 A.M. made all of the garbage from the three daily meals available to the mice throughout the night and most of the day. At the time of the outbreak the outer walls of the incinerators were found to be covered with mites, unfed or engorged.\* From a collec-

\* Between October 8 and October 14, 1952, a continuous record of the temperature of the outside wall of one of the incinerators was obtained by means of a thermocouple potentiometer recorder. The thermocouple was fixed to the wall of the incinerator, approximately five feet from the basement floor. During the outbreak numerous mites had been found on the wall of the incinerator at approximately this level. The furnaces were in

tion of mites taken on the walls of the incinerators *R. akari* were recovered.<sup>18</sup> Several mites were found in the vicinity of mouse runs beneath the kitchen cabinets. Mouse nests and runs were identified in the storage rooms in the basement and in the various apartments and apartment kitchens. A careful inspection of the apartments and kitchens indicated that the principal source of food for the mice was the contents of the incinerators, and the rest of the building served as very ample space for harborage and nesting. The mouse population had adjusted to feeding at one or both of these communal boards, which offered the advantages of easy accessibility, a quiet, secluded atmosphere broken only by the occasional descent of more manna from heaven, and almost 24 hour self-service. The conditions were such as to produce the maximal mixing of mice at the site most favorable for the multiplication of *A. sanguineus*.

#### DISCUSSION

There would seem to be little doubt that Rickettsialpox had existed in parts of New York City for some time prior to 1946. Although the widespread endemic distribution the disease now enjoys there may have taken years to develop, its progress in other cities where analogous conditions exist may be expected to follow a similar pattern.

At present we have little knowledge of the precise conditions which determine the activity of the disease at any endemic point or give rise to the isolated case. Between mouse and man *A. sanguineus* is certainly the weakest link in the chain in terms of requirements for conditions of survival. As such, one might expect that more exact knowledge of the habits and requirements of this mite would shed the most light on those factors having the greatest influence on the epidemiologic activity of the disease.

#### SUMMARY

The distribution of cases of Rickettsialpox has been considered in terms of the relationship of the habits of the house mouse and the mouse mite, *Allodermanyssus sanguineus*, to conditions of housing and differences in the living standard in various sections of New York City. At present this disease enjoys its widest distribution and greatest activity in the middle and upper income areas, where the density of housing is greatest, less in rat-infested slums, and least of all in those parts of the city where separated, smaller living units prevail.

use in the apartment and the superintendent fired the incinerators according to the schedule which had been in vogue at the time of the outbreak, once daily, at about 7:30 a.m. The record obtained was a slow undulating curve ranging between 68.5° F. and 75° F. The temperature of the outside incinerator wall fell below 70° F. during the night for periods ranging from three hours on one occasion to 10 hours on another. After one intentionally heavy firing it rose to 75° F. and fell only to 73° F. during the night prior to the subsequent firing. During the day when the apartment furnaces were in use the basement temperature ranged from 68° F. to 70° F. Spot measurements of the relative humidity in the vicinity of the incinerator were taken at various times during this six day period by means of a sling psychrometer. The relative humidity ranged from a low of 44 per cent to a high of 56 per cent.

## ACKNOWLEDGMENTS

The authors wish to express their appreciation to Dr. Morris Greenberg for his interest, suggestions, and cooperation in making available the addresses of reported cases of Rickettsialpox, as well as other sources of information required in this study, and to Mr. Clinton Garvin for information on rodents and housing in New York City. To Mr. Bruce Miller and Mr. Charles Wilkins, of the Instrument Division, United Aircraft Corporation, East Hartford, Connecticut, we are indebted for the temperature readings on the incinerator wall. To Mr. J. W. Huntington, Archt., we are indebted for the schematic section of the apartment house.

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## MEDICAL SIGNIFICANCE OF ILLNESS AND ABSENCE IN AN INDUSTRIAL POPULATION \*

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It is a fact that the practicing physician spends most of his time taking care of the sick person and, as a result, often knows very little about the well person. In medicine in industry, the same situation obtains, and again the industrial physician's experience is largely with the employee who is frequently ill and has high absence. In our studies of illness and absence in an industrial population, we have attempted to focus our attention equally on well employees with little absence and on sick employees with high absence. Perhaps it is even more important to know why well people are well than why sick people are sick. Certainly a comparison of the two groups is important.

Early in our observations we became impressed with how free from illness over long periods are the employees with the lowest absence and how continuously and frequently sick are those employees with the highest absence. The lowest-absence employees came to mean well employees, and the highest-absence, sick employees. We became impressed with how well were the well persons and how sick were the sick persons. A fact of considerable practical significance is how little medical attention is received by the "most well" and, on the other hand, how much medical service is rendered by physicians, surgeons, specialists, clinics and hospitals to the frequently ill individual.

A year ago, in a statistical study<sup>1</sup> of the absences of 1,297 women employees throughout their working careers, we confirmed previous reports that, in any one year, a high proportion of the absence, in terms both of number of days and of number of times absent, was caused by a small proportion of the employee population. This is shown in charts 1, 2, 3 and 4. Furthermore, we showed that employees with high-absence in their first year of employment were in the high absence group year after year (chart 5), while employees with low-absence in their first year as a rule remained in the low-absence group throughout their period of employment. Our studies showed that the absence pattern for an employee was almost as characteristic for that individual as his blood pressure or pulse or weight pattern. One might add that the absence pattern, like the weight pattern, is difficult but not impossible to alter. In this report we shall describe in some detail characteristics of the average low-absence person compared with those of

\* Presented at the Thirty-fourth Annual Session of the American College of Physicians, Atlantic City, New Jersey, April 14, 1953.

### TIMES ABSENT DURING FIRST YEAR OF SERVICE

#### WOMEN EMPLOYEES

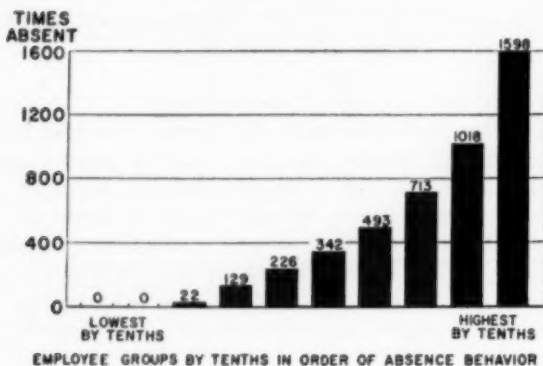


CHART 1.

the average high-absence person, and shall point out some of the medical, industrial and sociologic implications of our studies.

After collecting absence statistics on the larger population included in our studies for comparing the low-absence and high-absence persons, we made a random selection of 20 of the lowest-absence women employees with more than 20 years of service for comparison with 20 of the highest-absence

### DAYS ABSENT DURING FIRST YEAR OF SERVICE

#### WOMEN EMPLOYEES

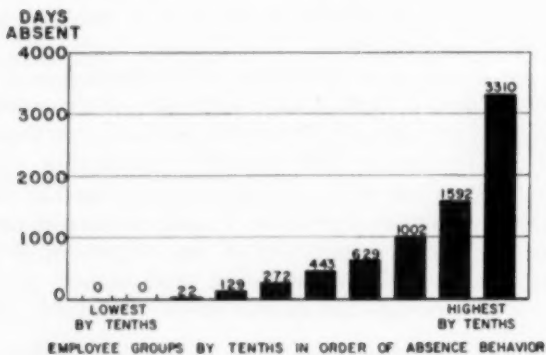


CHART 2.

## TIMES ABSENT DURING 1950

## WOMEN EMPLOYEES

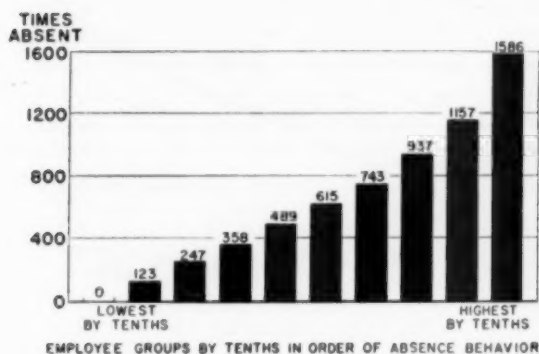


CHART 3.

employees with more than 20 years of service. In these 40 cases, all of the administrative data having to do with length of service, absence, transfers, etc., were analyzed. Next, we reviewed the confidential Medical Department records and tabulated the results of the initial applicant examinations and all subsequent visits and examinations. Some of these were in the nature of periodic examinations, but most had to do with examinations upon

## DAYS ABSENT DURING 1950

## WOMEN EMPLOYEES

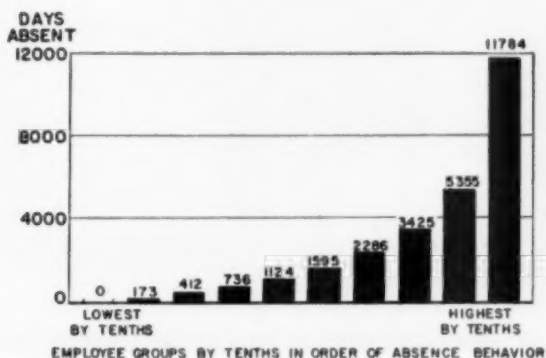


CHART 4.

**AVERAGE DAYS ABSENT PER YEAR FOR PERIOD OF SERVICE  
COMPARED WITH  
DAYS ABSENT DURING FIRST YEAR**

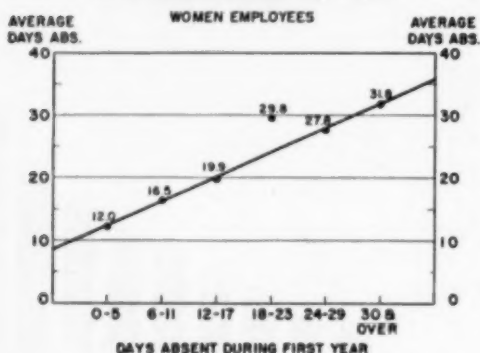


CHART 5.

return to work after illness. These medical records included reports from private physicians, specialists, clinics and hospitals. Because of the administrative requirements of our sickness benefit plan, these records included some notation in connection with all sickness absences of eight calendar days or more. The 20 low-absence records were small and quickly reviewed; on the other hand, the 20 high-records were voluminous and required days to review and tabulate (figure 1).

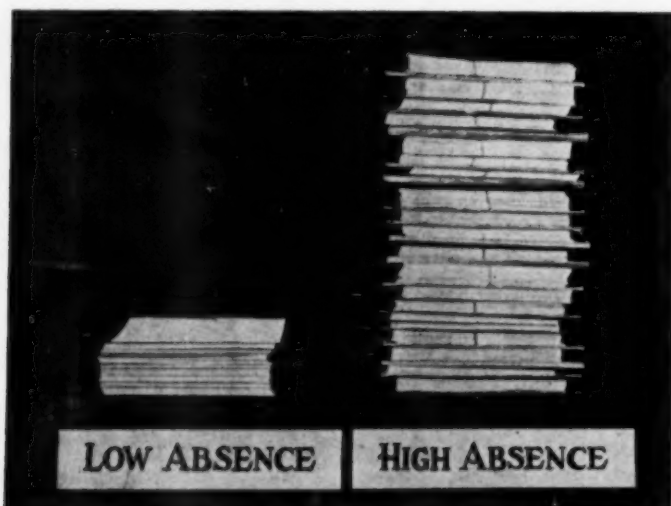


FIG. 1. The medical records of the 20 low-absence employees and the 20 high-absence employees compared in this study.

In addition to our analysis of both the administrative and the Medical Department records, each of these 40 women employees was seen in the Medical Department by my associate, Dr. Hinkle. Each was interviewed at length regarding not only her medical but also her family history, her cultural, economic and social background, as well as her present life situation. Careful note was made of any evidences of disturbance of mood, thought and behavior. These interviews, whenever possible, were supplemented by physical examination and laboratory and other diagnostic studies.

Charts 6, 7, 8, 9, 10, 11 and 12 and table 1 show a comparison of over-all figures regarding systemic illnesses, accidents, operations and contacts with the Medical Department of each of the two groups of 20 employees. At

### RESPIRATORY DISORDERS WOMEN EMPLOYEES

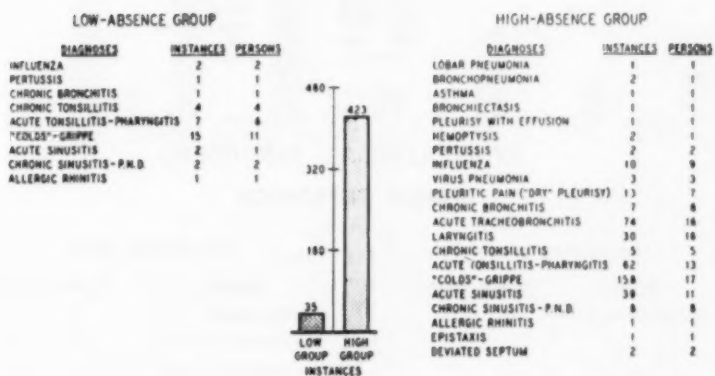


CHART 6.

this point, however, we should like also to compare the average low-absence employee with the average high-absence employee.

The average low-absence woman employee (L. A.) is 48 years old, single and has worked 28 years for the company. She had had the usual childhood diseases, and when she started working for the company at age 20 her pre-placement examination revealed no significant physical defects. During her entire 28 years with the company she had had only 33 days of absence. This average low-absence employee lost eight days one winter when she had an accident, such as spraining her ankle and contusing her hip from slipping on the ice. The other two absences probably were due to a bad cold and acute sinusitis, from which she recovered in two weeks, and an absence of 10 days due to an attack of nausea, vomiting and diarrhea. She probably would

# DISORDERS OF FEELING STATE, THOUGHT AND BEHAVIOR WOMEN EMPLOYEES

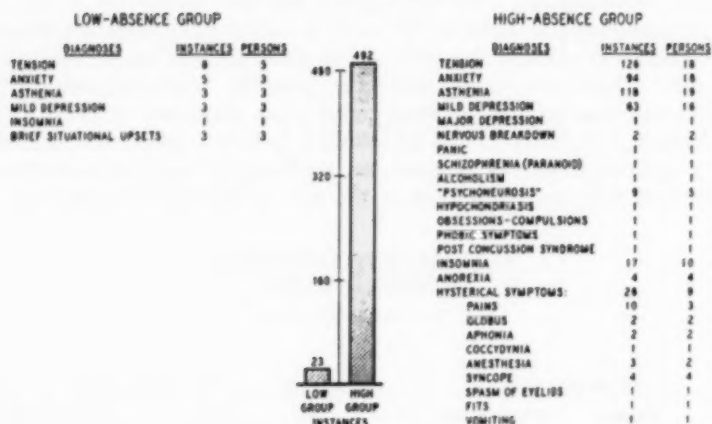


CHART 7.

# GYNECOLOGICAL DISORDERS WOMEN EMPLOYEES

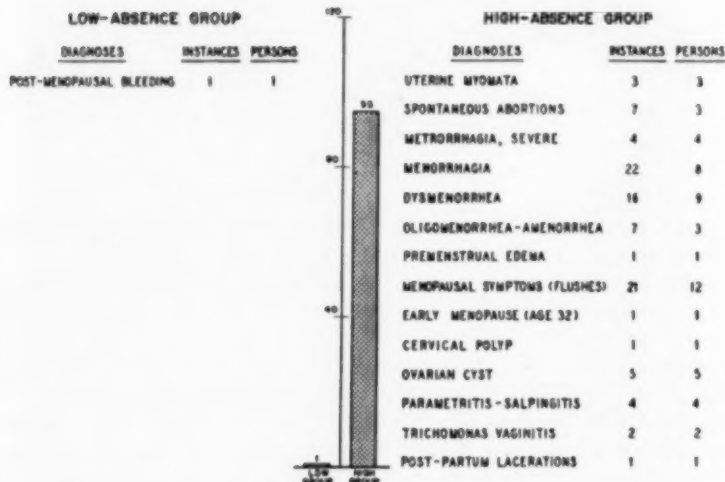


CHART 8.

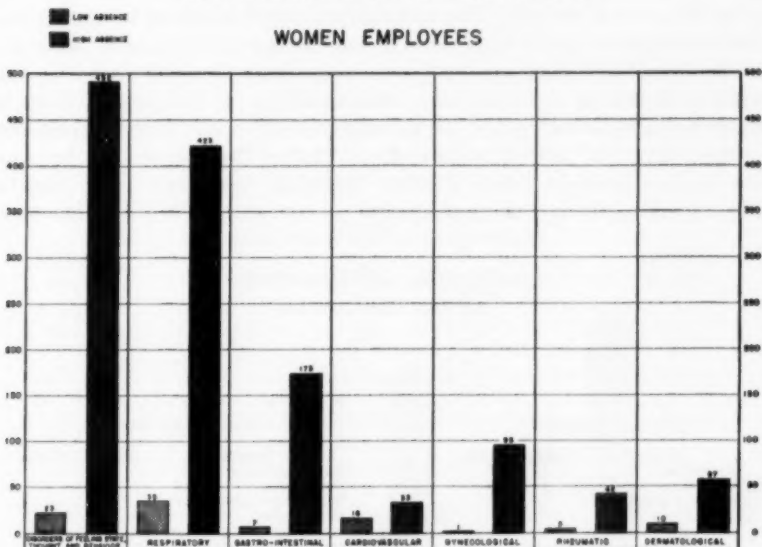
COMPARISON OF SYSTEMIC DISEASES IN THE  
LOW ABSENCE AND HIGH ABSENCE GROUPS

CHART 9.

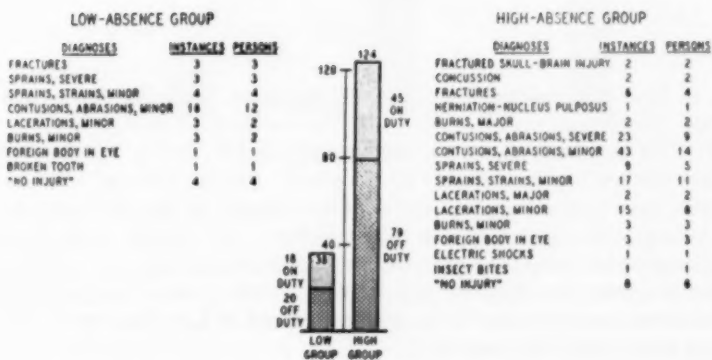
ACCIDENTS  
WOMEN EMPLOYEES

CHART 10.

have returned to work sooner following this latter episode but her physician requested that she stay off duty until she had had a gastrointestinal series and barium enema x-rays. The low-absence employee never in her 28 years with the company had absence from dysmenorrhea or from colds other than the one described, which probably was complicated by acute sinusitis. She denied ever having dysmenorrhea, and although at the present time her periods probably are irregular, she is having no nervous or tension symptoms. She does have two or three mild colds a year but they never keep her away from work. Also, at times she has had mild headaches. She has had much dental work, including a number of extractions, but she has found

### SURGICAL OPERATIONS WOMEN EMPLOYEES

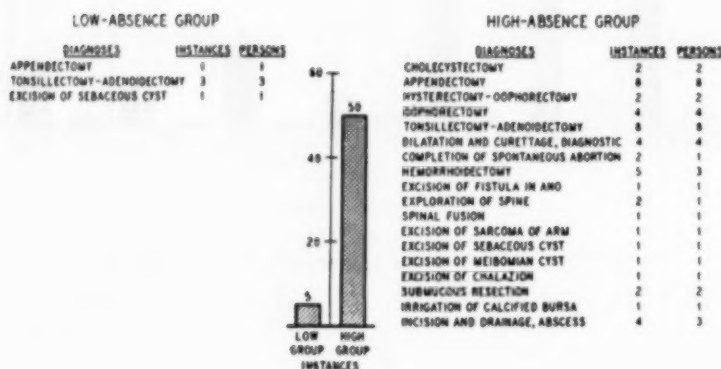


CHART 11.

ways to have this done after work or on Saturday. She has never had any surgical operations.

The average high-absence woman employee (H. A.) is 46 years of age and has worked for the company for 26 years. On the average, she has been divorced once and married a second time. Again on the average, she has two children for whom she takes responsibility. Her family medical history is not significant, and she had no unusual children's diseases. When she started working for the company at age 20 she passed the preplacement examination, and nothing in the medical record at that time gave any clue to poor future health prospects.

This average high-absence employee during her 26 years of employment has had 1,209 days of absence. In all but four years her absence has been

excessive, ranging from three weeks to one year, in which she was absent continuously for the whole year. In addition to her long absences, she has had numerous incidental absences lasting two to three days.

During the 26 years she has had two major and four minor accidents, three of these having occurred while on duty. Because of the six accidents she lost 109 working days. She had three operations, two major and one minor. During the time that she was out for a complete year she probably

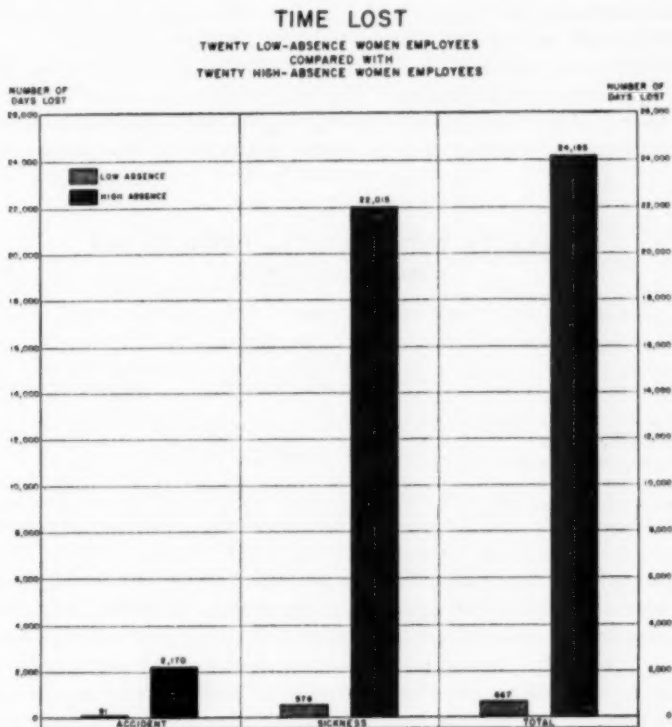


CHART 12.

had a severe respiratory infection, such as pneumonia and pleurisy, and also had one of the major operations. For the last two months of this year of disability she probably had fatigability and headaches, and her doctor did not think she was well enough to return to work. In addition to the severe respiratory attack, this employee had 19 other absences because of other respiratory infections such as colds and grippe. She had seven gastrointestinal episodes, each causing an absence of more than eight days. One of these disabilities lasted three months, probably because her doctor sus-

pected that she had an ulcer. This employee has had frequent attacks of dysmenorrhea and has frequently lost time for this reason. When she was about 40 she probably had a complete hysterectomy and at this time was absent for about six months. This employee at one time was probably treated for low blood pressure, which was said to be the cause of her fatigability, headaches and inability to work. At another time she was out because of low back pain. At still another time she was disabled because of neuritis or perhaps bursitis of her shoulder. Also, at one time she probably had something like herpes zoster, and at other times cellulitis of her left arm and several episodes of absence because of small carbuncles.

On interview, our low-absence employee (L. A.) was found to be a happy and contented individual. She was "outward going" and capable of diffuse emotional attachments, having few preconceived notions of what she wanted to do. From time to time opportunities for promotion had

TABLE I  
CONTACTS WITH MEDICAL DEPARTMENT  
WOMEN EMPLOYEES

	LOW-ABSENCE GROUP	HIGH-ABSENCE GROUP
MEDICAL DEPARTMENT VISITS	380	2,927
CERTIFICATES FROM PRIVATE PHYSICIANS	16	311
INVESTIGATIONS OF ILLNESS	15	188
FREQUENT ILLNESS INVESTIGATION	0	28 (8 PERSONS)
VISITS TO REST HOME	2 (2 PERSONS)	37 (13 PERSONS)

developed for her, but she felt happier with the lack of responsibility and the easier hours which she had attained in her present position. She had only a few outside interests and her life was a very simple and orderly one. Her career was her job. In the past, when she had been moved from one type of work to another or from one location to another, she rapidly adapted herself to the change. L. A. was well liked by her associates and her supervisor because of her capacity to make friends, her failure to complain and her pliability with regard to her assignments.

H. A. (average high-absence employee) on interview was found to be unhappy, discontented and resentful. She had few friends and drew little sustenance from the group in which she worked. She became easily frustrated and unhappy when she was forced to deviate from her goals or her position in life. She had many responsibilities outside of her job, including those for her home and children, and she often developed a resentment towards her family and friends similar to that which she showed towards her job and her supervisors. When in the past she had been transferred

from one job to another or from one office to another she had reacted with distaste and complaints. She resented it when promotions had not been offered to her. Because of her unhappiness she welcomed any legitimate excuse to absent herself from work. Sometimes she seemed to tolerate her symptoms and return to work, but only because of the presence of economic necessity. H. A. was not liked by her associates and supervisors because she was not friendly, was always complaining, and was not reliable or pliable in regard to her assignment.

From this comparison, it is obvious that we in industry appreciate the reliability and flexibility of the low-absence employee and, on the other hand, recognize an increasingly serious problem in dealing with the high-absence employee. We have pointed out that as a rule the doctors in the Medical Department scarcely know the low-absence employee, while at the same time the facilities of the Medical Department are taxed in examining, investigating and managing the high-absence employee.

To return to L. A., our low-absence employee, we find that she visited the Medical Department only 18 times during her entire 28 years with the company, while H. A. in her 26 years of service visited the Medical Department 146 times and had large numbers of x-rays, laboratory tests and consultations. Numerous reports were sent to her private physicians regarding the results of diagnostic examinations, and many certificates were filled out for her supervisors regarding when and under what conditions she could return to work.

How should the company or, more specifically, the company Medical Department, cope with this problem?

1. *The high-absence cases should be recognized early.* First of all, the concept of concentration of illness and absence in a small segment of the population should be fully appreciated. Accurate attendance records, together with careful interviews, become the chief methods for recognizing the cases early. Physical examinations, x-rays and laboratory tests, while important in ruling out significant organic disease, do not make the diagnoses in these cases.

2. *The high-absence cases when recognized should be fully evaluated.* The greatest hazard is to consider each episode of cold, headache or gastrointestinal upset separately and independently and not to appreciate it as part of a chronic and repetitive disease related to the reactions of the particular individual to certain situations and stresses in life.

3. *These high-absence employees must be studied and managed.* Their management is difficult but not unsurmountable. It entails, among other considerations, proper interviewing and counseling, and sometimes firm disciplining of the individual employee. Training and education of supervisors, and a flexibility and willingness on the part of management to help an employee alter distressing situations. Today, most of this is what industry calls its human relations program.

The private physician is very much involved in this absence problem. Again, we note from our study that L. A. rarely saw her private physician. However, in the 26 years that H. A. worked for our company we know that she saw her private physicians and specialists numerous times. H. A.'s private physicians talked with our doctors in the Medical Department on the telephone nine times and furnished us with 16 certificates of illness. Also, a number of times they furnished so-called doctor's lines, recommending change of work, or shorter hours, or requesting disability leave for a rest in the country, or Florida. H. A.'s surgeons performed two major and one minor operations, besides treating her for two major and four minor accidents. Incidentally, her private physician filled out a number of workmen's compensation forms for her and testified twice for her before the Workmen's Compensation Board. Her private physicians and specialists treated her grippy colds, sinusitis, bronchitis, gastrointestinal disturbances, dysmenorrhea, menopausal syndrome, palpitation, neuritis and herpes zoster. They prescribed quantities of medicine and gave her many injections, and at times were at their wit's end because, after all the pain, cough and rash had subsided, there were still the nervousness and fatigability which kept her from being well and returning to work.

The initial problem for the private physician is the same as for the doctor in industry, namely, early recognition of the case and a proper understanding of the disease. The private physician should put emphasis on treating the underlying disorder. He also must appreciate the variations in the emotional and nervous status of individuals and the different reactions that occur from various situations, stresses and strains. If the private physician and the specialist understand the underlying problem they will find that fewer operations and injections will be indicated and less drug therapy will be used. Again, the private physician will find that the treatment of the nervous and emotional symptoms and the associated bodily disorders is difficult but not unsurmountable, and that the results can be very rewarding. It is tempting to believe that all of these patients are psychoneurotics<sup>2</sup> or hysterics.<sup>3</sup> Another pitfall for the private physician is the belief that all illness is functional in origin. He may then miss the early diagnosis of cancer, heart disease, tuberculosis, and neurologic and endocrine diseases, and may be doing irreparable harm by delaying important surgery and other definitive treatment. So the road ahead for the physician is not an easy one.

We cannot end this report without mentioning briefly the implications of these findings for our society and our economy. Our low-absence employee had very little need for clinics, hospitals and other medical institutions. She had Blue Cross and Blue Shield insurance but seems never to have used it. The state sickness disability insurance and workmen's compensation insurance have meant nothing to her. On the other hand, H. A. was in and out of clinics, hospitals and other medical institutions, just as she was in and out of work. Undoubtedly, she has been very costly to the Associated

Hospital (Blue Cross) and United Medical (Blue Shield) Services. Also, she has been very costly to the company because of the charge levied on it for the state sickness and workmen's compensation insurance.

While this report was being written the New York newspapers were carrying this statement: "He (Governor Dewey) noted that employers in New York paid \$300,000,000 a year for workmen's compensation insurance."<sup>4</sup> The protection of this insurance is spread over the working population, but from observations such as ours there is every evidence that the compensation expenditures, like our industrial absences, are concentrated on a small segment of the working population. The state workmen's compensation boards might well study this problem to see what can be done about it. The United Medical Service Bulletin for March<sup>5</sup> showed that in Greater New York City in 1952 a sum of \$18,562,834.77 was distributed to physicians for service to United Medical Service subscribers. Again the likelihood is that, on a year-to-year basis, this is not at all a smooth distribution of payments among all persons and families. Again, this problem deserves consideration. Finally, the March, 1953, Bulletin of the Common Cold Foundation<sup>6</sup> carried this statement: "We know that an average of 7,000,000 persons are incapacitated each day of the year because of the 'common cold.' We know that 150,000,000 to 180,000,000 man-days are lost by industry and business annually, to say nothing of the man-days lost in our armed forces and in our schools and colleges. We know that business and industry lose over \$4,000,000,000 annually in production, services, and wages." We have great respect for the cold virus and we subscribe to the belief that it is one of the factors in the etiology of "colds." However, we know it is not so costly as this. Again from such studies as ours, there is every likelihood that this \$4,000,000,000 problem is tied up with an underlying condition that has more to do with situational problems, motivation and attitudes than with the cold virus.

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## CASE REPORTS

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### FATAL ADRENAL CORTICAL INSUFFICIENCY PRECIPITATED BY SURGERY DURING PROLONGED CONTINUOUS CORTISONE TREATMENT\*

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#### INTRODUCTION

WHEN hyperadrenocorticism is deliberately induced with ACTH or cortisone for the control of disease, the resulting changes in disease activity are accompanied by a wide variety of physiologic and metabolic changes, some desirable and others unfavorable. Among these are alterations in the function of the anterior pituitary and the adrenal cortex, two endocrine glands of major importance in maintaining the ability of the body to withstand many different types of stress. The increased blood glycocorticoid level which cortisone induces directly and which ACTH produces by adrenal stimulation leads to an inhibition of the output of endogenous ACTH by the pituitary. During prolonged cortisone treatment, the diminution in endogenous ACTH output and the resulting decrease in adrenal stimulation lead to marked hypoplasia of the adrenal glands. Long-term treatment with ACTH produces no decrease—or even some increase—in adrenal size because the exogenous ACTH given more than compensates for the diminished output of ACTH by the pituitary.

The sudden withdrawal of cortisone after prolonged administration may produce a prompt and serious relapse in the primary disease, associated with signs and symptoms resembling those of adrenal cortical insufficiency. These disturbances appear to result principally from the inability of the hypoplastic adrenal cortex to respond promptly to increased ACTH stimulation, rather than from failure of the pituitary to secrete ACTH. Thus, several days of intravenous ACTH treatment may be required to restore normal adrenal responsiveness to a patient whose adrenals have been rendered hypoplastic and hyporesponsive by long-continued cortisone treatment. The inhibition of pituitary ACTH output which occurs during long-continued ACTH treatment is apparently less significant. Withdrawal of ACTH seldom leads to the prompt relapses in disease and quasi-Addisonian state induced by sudden cessation of oral cortisone treatment, possibly because the increased responsiveness of the patient's adrenals partly compensates for lessened pituitary ACTH output. The most severe and acute

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exacerbations of disease and pictures closely resembling fulminating Addisonian crisis occur after sudden withdrawal of oral cortisone. Sudden withdrawal of intramuscular cortisone has less serious consequences because the patient is partly protected by a depot of slowly absorbed cortisone in the muscle.

In recent months there have been increasing indications that a sudden increase in the demand for adrenal cortical steroids may have serious consequences for the patient whose pituitary-adrenal mechanism has been rendered unresponsive to stress through prolonged use of cortisone. A recent editorial, published since our experience with the case to be reported, has emphasized the risks incurred when surgery is performed during the course of cortisone therapy.<sup>1</sup>

The case reported is one in which an uneventful corrective procedure was followed promptly by adrenal cortical insufficiency in a patient who had received moderate daily doses of oral cortisone for a six month period extending up to the day of operation. It emphasizes the fact that adrenal insufficiency in such a patient may be induced not only by withdrawal of oral hormone but also by the failure of such a patient's pituitary-adrenal system to respond to operative stress by increasing glycocorticoid output. It thus illustrates the importance of providing preoperative protection through pretreatment with ACTH whenever anesthesia or surgery becomes necessary in patients receiving prolonged maintenance dosage of cortisone for rheumatoid arthritis or other disorders. By implication, it strongly suggests the importance of considering similar supplements whenever a medical or surgical emergency must be met by an individual receiving long-term cortisone treatment.

#### CASE REPORT

A 20 year old white woman was admitted to a rehabilitation center for the treatment of chronic disabling rheumatoid arthritis on August 27, 1951. In 1946 she first had localized joint swelling, pain and superficial bleb formation on the left great toe. This cleared after two months, leaving her symptom-free for a brief interval before the onset of acute swelling of the left knee and left wrist, and pain and swelling of the neck region.

With the onset of illness she had fever and sweats, and these symptoms later accompanied each exacerbation of joint disease. Although intermittent acute attacks of arthritis occurred, she was never without some joint involvement following her initial polyarthritis. Ultimately, the disease spread to the elbows, wrists, knees and ankles bilaterally. The spine, fingers, hips and toe joints remained fairly free. Occasionally she had pain in the jaw and also some backache, but range of spinal motion was never greatly impaired. During early 1950 she developed an acute attack involving both knees, which lasted several months and finally resulted in marked limitation of motion with inability to extend either leg beyond 90 degrees.

The past and family histories were not significant. Arthritis was not known to have occurred among members of her family.

Physical examination revealed no abnormalities which could not be related to the musculoskeletal system. Respiratory excursion was limited, and vital capacity was 1.6 L., or approximately 46 per cent of normal for the patient's age and height. Spinal motion was somewhat limited, particularly in the lumbar region. Both elbows showed limitation of extension and flexion, the left more than the right. Right wrist motion was also somewhat limited. Hip motions were only slightly restricted. The right knee moved between 45 and 88 degrees, and the left between 70 and 80 degrees of flexion. Both ankles were slightly limited. The proximal interphalangeal joints

of the right second, third and fourth fingers showed some spindling and minimal limitation of motion. The left ulnar-carpal region was swollen, and the left wrist crepitated on motion.

Treatment regimen consisted at first of planned physical and occupational therapy, together with the use of simple analgesics. Cortisone therapy was begun on November 2, 1951 with an oral dose of 25 mg. four times daily for 14 days. The dosage was then progressively diminished between December 5 and December 17, at which time she received 62.5 mg. daily in divided doses. During the remainder of the treatment period she received between 62.5 and 100 mg. of cortisone daily in divided doses. The most satisfactory maintenance dose was 75 mg. Throughout the period of cortisone treatment she also received potassium chloride in the form of enteric coated tablets, 0.9 gm. three times daily, and thyroid extract, 0.03 gm. daily, from February 12 to February 27, 1952, and 0.06 gm. from February 27 to March 17. The total amount of cortisone administered was 8.5 gm.

The patient showed an excellent response to combined physical and steroid therapy. Joint mobility increased progressively, and ultimately only the contractures of the knees remained to produce significant orthopedic deformity. Periodic hematologic studies revealed no abnormalities. The blood sugar level remained fairly constant. Urinalysis was repeatedly negative. There were no indications of toxicity or hypercorticism at any time. As an indication of joint improvement, the right elbow, which previously extended to only 130 degrees, increased in range of extension by 30 degrees. Both shoulders showed increased motion, tenderness and pain in all peripheral joints disappeared, and backache was no longer experienced.

To complete the rehabilitation of this patient, it was considered important to attempt to improve knee function to permit ambulation. Physical therapy included techniques designed to increase muscle strength in the knee extensors and to extend the range of joint motion. Although there was less pain on attempted stretching, the increase in mobility was relatively slight after six months of therapy. Plaster casts were then applied to both lower extremities, with the object of attempting gradual extension with the use of turnbuckles. This method was not successful because of the patient's intolerance of the casts. After more conservative means were exhausted, surgery was considered to be essential to increase joint excursion for ambulation. In the opinion of the orthopedist (R. R.), this could be achieved either by performing wedge osteotomies at the lower ends of the femurs, or by posterior capsulotomy and tendon lengthening of the posterior thigh muscles at both knees. The latter procedure was considered most suitable, and the patient was scheduled for surgery.

*Operation:* On March 18, 1952, under sodium pentothal induction and inhalation nitrous oxide anesthesia, the patient underwent a two and one-half hour surgical procedure consisting of posterior capsulotomy and tendon lengthening of the right knee to correct flexion contracture. To close the incision a full thickness pedicle skin graft was swung from the posterior surface of the right thigh down over the popliteal area. The operation was uneventful except for expression of about 100 c.c. of accumulated blood in the popliteal space after closure, which prompted re-opening of the incision. No active bleeding was discovered. Capillary oozing was controlled by pressure dressing and a posterior plaster splint.

Throughout the operation the blood pressure remained between 120-100/80-70 mm. of Hg, and the pulse rate between 80 and 90 per minute. During surgery the patient received 500 ml. sodium lactate solution and 250 ml. per cent dextrose in normal saline intravenously. She was sent to the ward in good condition, with a blood transfusion running. Upon her return from surgery the blood pressure was 90/60 mm. of Hg, the pulse rate 100 per minute.

*Postoperative Course:* One-half hour after return to the ward the patient became very restless, thrashed about and disconnected the blood transfusion. The pulse

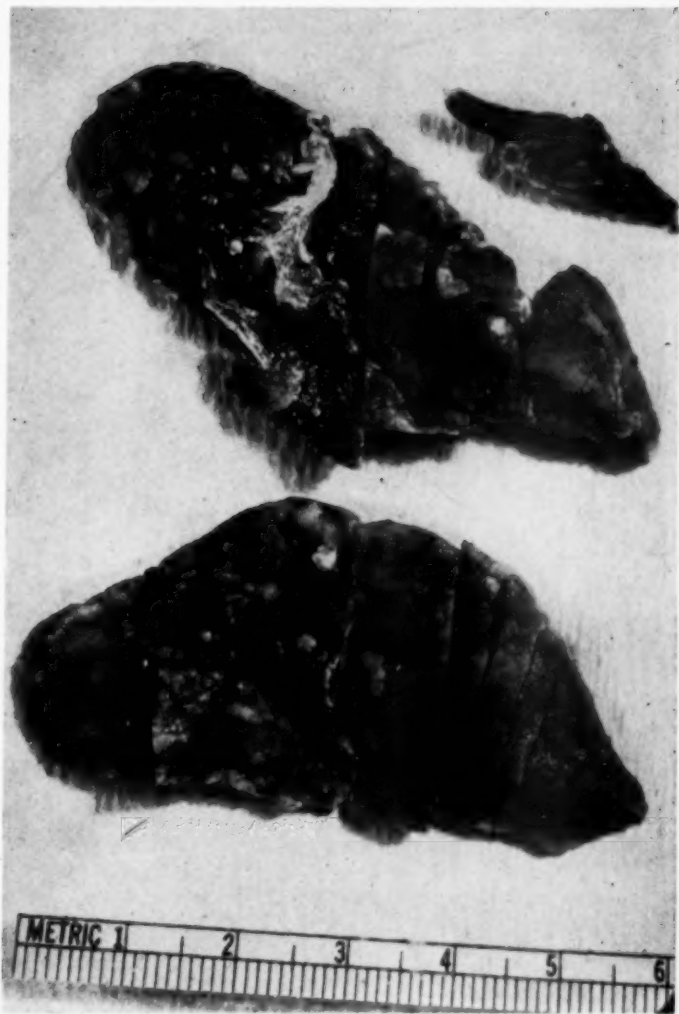


FIG. 1. Right and left adrenal glands after fixation. The dark discoloration represents hemorrhage and congestion.

became thready, rapid and uncountable, and blood pressure could not be obtained. The skin was cold and cyanotic, respirations were short and rapid. With intranasal oxygen and re-institution of the blood transfusion, color improved and the pulse became stronger. Following the apparent improvement in condition, the patient again became restless and the blood transfusion was interrupted, with worsening of condition. A cut-down was established and blood transfusion re-instituted. There was again reassuring return of good skin color and strong pulse.

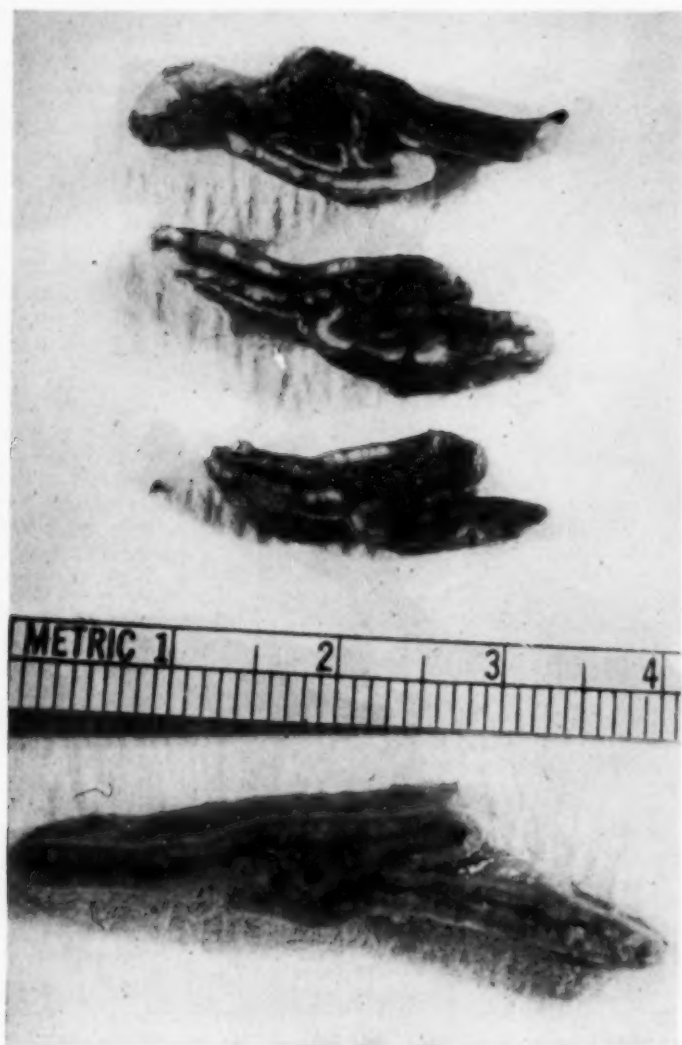


FIG. 2. Three upper sections from adrenals in case reported are compared with cross section of a normal gland below.

Two hours postoperatively the patient became hyperpyrexia and had a very flushed skin. There was no chill. The pulse rate rose to 164 and the respiratory rate to 48 per minute. The lungs remained clear; no pleural rubs were heard. There was no hemoptysis or evidence of pulmonary congestion. No excessive bleeding occurred from the operative site. The patient remained very restless, requiring restraint. She

was able to ask for water and coffee on occasions, but was never mentally clear. Five and one-half hours postoperatively, Cheyne-Stokes respiration set in. Thrashing ceased, and in spite of intranasal  $O_2$ , artificial respiration and stimulants, the patient died five and three quarters hours postoperatively. She had received a total of 1,000 ml. of whole blood, and 1,000 ml. of one sixth molar lactate, 1 gm. of aureomycin, 200 mg. of vitamin C and 10 mg. of Hykinone intravenously post-operatively.

*Autopsy:* The significant findings, aside from arthritic deformities of the spine, left upper extremity and right knee, were as follows: The right lower extremity was in full extension. A recent "C" shaped surgical wound with convexity directed medially extended from the mid thigh to the popliteal region. A cigarette drain was in situ near the inferior pole of the incision. A small hematoma was present under the right superior parietal scalp.

With the exception of the adrenal glands the viscera showed no striking gross abnormalities. A streak of subendocardial petechiae was noted along the septum in the left ventricle. The myocardium was a slightly pale brownish red. The lungs

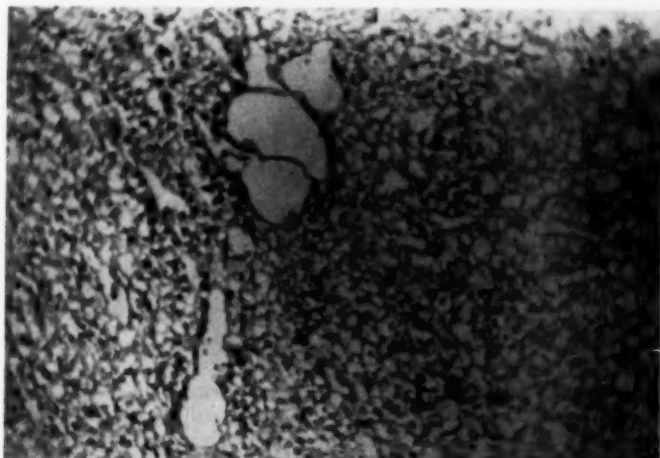


FIG. 3. Relatively cellular area of adrenal gland, showing large vacuolated cells.

were fully aerated and somewhat hyperemic. The kidneys also appeared injected.

The adrenal glands were both somewhat smaller than normal and showed marked atrophy of both the cortex and medulla bilaterally (figures 1 and 2). The total weight of both glands was 8.0 gm. What appeared to be gross hemorrhage was visible on the surface as well as in cut sections. The left gland showed most extensive discoloration by blood, but both glands had numerous areas of apparent hemorrhage and marked congestion involving both the cortex and medulla. The pituitary gland appeared normal in size but was markedly hyperemic. The cerebral blood vessels were injected but the brain was otherwise normal in appearance.

Histologic examination showed generalized visceral hyperemia but no other changes of importance in any of the organs except the adrenals. The pituitary gland showed normal morphology of the anterior lobe, with a rich vascular supply and some hyperemia. The median portion showed the usual somewhat prominent fibrous stroma and a few dilated colloid-filled acini lined by cuboidal cells. The posterior lobe had the usual glial structure. Some cells had fine brown pigment granules in

the cytoplasm. Occasional small masses presumed to be colloid were noted. There was a fairly rich supply of fine capillary vessels. The histologic appearance of the hypophysis was considered normal.

Paraffin sections of formalin-fixed adrenal tissue stained by hematoxylin and eosin showed marked degeneration of the entire parenchyma (figures 3 and 4). Most of the cells were lysed and were represented by open spaces. Some of the cells had persistent nuclei with the cytoplasm absent, while others had remnants of cytoplasm with some fibrin threads visible in it. The remaining well defined nuclei were regular in appearance and fairly well stained.

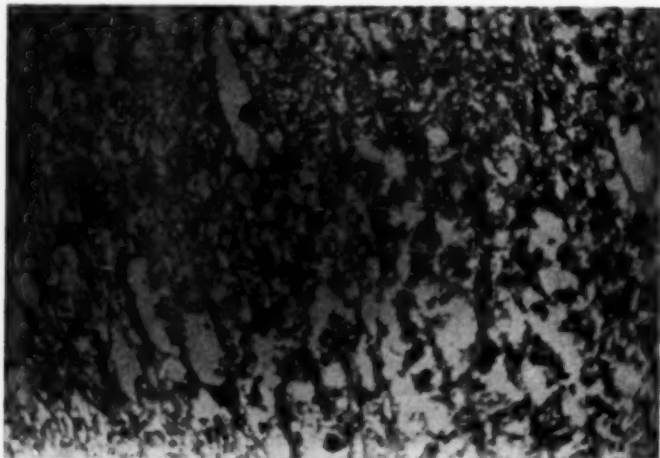


Fig. 4. Area of marked cellular atrophy and hemorrhage within the adrenal gland.

The connective tissue architecture was retained so that the epithelial cord outlines could be seen, although the zones could not be clearly differentiated. The capillaries were dilated with blood, and the organ appeared much more vascular than normal; some red cells were found free in the vascular spaces. The medulla could not be distinguished. The capsule was well formed and intact, and paracapsular fat was typical.

#### COMMENT

Upon superficial examination the adrenals in this case appeared to be frankly hemorrhagic and the lesion was considered to be quite characteristic of the Waterhouse-Friderichsen syndrome. However, histologic section revealed that there was very much more to the pathologic lesion than simple hemorrhage of the adrenal cortex. The cortical cells were atrophied almost to the point of disappearance, and no medullary tissue could be made out. (Complete serial sections were not studied. Therefore, the absence of adrenal medulla may be an artefact.) Throughout the remaining vacuolated cortical cells there were many dilated capillaries containing blood, as well as fresh blood within the vacuoles and intercellular spaces.

In order to try to analyze the basic pathogenesis of the adrenal lesion described, it is necessary to review the physiologic effects of exogenous cortisone. It has

been well demonstrated that the administration of cortisone leads to suppression of pituitary function, particularly with respect to the secretion of adrenocorticotrophic hormone. This, in turn, leads to secondary adrenal cortical atrophy. In cortisone-treated patients the adrenal can be stimulated to resume production of hormone by exogenous ACTH. However, the adrenal response occurs only after a latent period which may last for several days. Thereafter, the adrenal apparently resumes its normal secretory function.

When cortisone is withdrawn rapidly from patients under maintenance regimens the persistent underfunction of the pituitary-adrenal system results in characteristic asthenia. This is particularly prominent following oral administration of cortisone, since utilization is prompt and no depot is established as in the case of parenteral administration.

While the above considerations are fairly well accepted explanations of the physiology of the pituitary-adrenal system, the explanation of the type of reaction observed in this patient is not apparent. If it is assumed, as is probably correct, that both the pituitary and the adrenal are rendered incapable of adequate response to stress by prolonged cortisone therapy followed by its rapid withdrawal, then the observed congestion and hemorrhage of the adrenal gland cannot be attributed to the overproduction of ACTH during the stressful period. It follows, therefore, that some other mechanism must be involved which represents either a primary or a secondary safeguard against systemic stress and which—even in the absence of ACTH secretion—produces a powerful stimulus upon the adrenal glands.

A clue as to a possible mechanism is suggested by the observations reported by Engel,<sup>2</sup> who showed, at least with respect to nitrogen catabolism, that stress can operate upon the organism by some means other than the stimulation of the adrenal cortex by ACTH. The exact physiologic modality is unknown, and there is no indication as to whether the influence is endocrine or neurogenic. In any event, there is evidently residual capacity for profound vascular response in an organ which is rendered incapable of physiologic response. There is a possibility that the vascular dilatation and hemorrhage are manifestations of a generalized histamine-like reaction in which the adrenal participates to a greater degree than other tissues.

Adrenal hemorrhage following major stresses is known to occur in persons with presumably normal endocrine function. The adrenal lesion following fulminating infection such as meningococcemia (Waterhouse-Friderichsen syndrome) and the adrenal and pancreatic hemorrhages following surgical procedures<sup>3</sup> or after obstetrical difficulty<sup>4</sup> have been interpreted as abnormal responses to excessive outpouring of adrenocorticotrophic hormone by the stimulated pituitary gland. Selye<sup>5</sup> discussed the relationship between the Waterhouse-Friderichsen syndrome and other types of adrenal cortical necrosis and hemorrhage, and supported the view that excessive stimulation of cortical cells by corticotrophins was responsible. This theory is untenable because of the repeated observation that massive doses of intravenously administered ACTH have not resulted in adrenal hemorrhage and death in animals or man. These observations strongly suggest that some mechanism other than adrenocorticotrophic response plays a significant rôle in either primary or secondary reactions to extreme stress.

In the case reported an alternative explanation is possible. Marked stress may overcome the pituitary inhibition exerted by cortisone, and the vascular response observed in the adrenals may be the earliest manifestation of adrenal stimulation by corticotrophin. The patient would have died, therefore, before adequate adrenal steroids were being produced. This explanation would not suffice, however, to explain adrenal hemorrhages in stress as a result of corticotrophin overproduction.

Although an additional and possibly more primitive generalized response to critical situations is implied by the foregoing discussion, it should be pointed out that, in the event of extreme demand upon a depleted pituitary-adrenal system, patients fail to survive only because of the unavailability of cortical steroids. If these are supplied in adequate amount by precise preoperative and postoperative programs, the probability for survival is greatly increased.

Accordingly, in order to prepare patients under treatment with cortisone or ACTH for elective surgery, a program similar to the one presented below is suggested.

The dosage schedule is modified as circumstances require and will depend in part, in the case of adrenocorticotrophic therapy, upon the particular preparation in use as well as the maintenance dose in each individual patient.

#### I. For patients receiving cortisone:

##### A. Preoperative program:

1. ACTH in doses of 20 to 30 units intramuscularly every six hours for five days before surgery.  
*or*  
ACTH in doses of 20 units, by slow intravenous drip (in 1,000 ml. 5 per cent glucose in water) over periods of 12 to 24 hours daily for three days before surgery.
2. Cortisone intramuscularly, 100 mg. daily for two days before surgery and again preoperatively on the day of surgery.

##### B. Postoperative program:

1. Normal saline, 1,000 ml. intravenously (or fluids as indicated by electrolyte and hematologic studies).
2. Cortisone intramuscularly, 25 mg. every six hours for three days or equivalent amount orally; then resume preoperative oral dosage.
3. ACTH in doses of 20 units intramuscularly every four to six hours for two days, then 15 units every six hours for two days, 10 units twice daily for two days, 5 units twice daily for one day (or modified schedule of gradually diminishing dosage).

#### II. For patients receiving ACTH:

##### A. Preoperative program:

1. Cortisone intramuscularly, 100 mg. daily for two days before surgery and again preoperatively on the day of surgery.
2. Continue usual ACTH dosage uninterruptedly.

**B. Postoperative program:**

1. Normal saline, 1,000 ml. intravenously (or fluids as indicated by electrolyte and hematologic studies).
2. Cortisone intramuscularly, 25 mg. every six hours for two days, then every eight hours for two days. If oral medication is possible at the end of a few days, continue with 25 mg. every 12 hours for two days, then 25 mg. daily for two days. Otherwise, follow the same dosage schedule by intramuscular route.
3. Continue usual (preoperative) ACTH dosage uninterruptedly.

III. For emergency surgery when above preoperative preparation is impossible, continue usual dosage of hormone and give 300 mg. cortisone intramuscularly. Also give 30 to 50 ml. of aqueous adrenal cortical extract intravenously during surgery, repeated if necessary. Postoperatively, give both ACTH by intravenous route and cortisone intramuscularly. The dosage required under these circumstances cannot be estimated accurately, but effective amounts should be used and electrolyte balance should be closely supervised.

**SUMMARY AND CONCLUSION**

1. The fatal outcome of a relatively routine surgical procedure in a patient under prolonged cortisone therapy for rheumatoid arthritis is reported.
2. Death resulted from acute congestion and hemorrhagic infiltration of adrenal tissue made atrophic by exogenous cortisone. The acute reaction and death were probably attributable to the stress of general anesthesia and surgery, superimposed upon cortisone-induced adrenal insufficiency and failure to supply large amounts of cortisone postoperatively.
3. The urgency of adequate preparation and hormonal support of cortisone treated patients during periods of extreme stress is impressively illustrated.
4. Because of the wide use of adrenal and pituitary hormones for treatment of a great variety of diseases, there will undoubtedly often be need for surgical intervention during the course of hormone therapy. The potentialities for disaster should be widely known. The need for close coöperative integration between the internist and the surgeon is clear.
5. A régime for preoperative and postoperative management of cortisone and ACTH treated patients is suggested.
6. Patients under cortisone therapy, or their responsible guardians, should be warned as to the possible consequence should they fail to receive additional supportive hormone in the event of accidental injury or emergency surgery. In emergency surgical services, careful inquiry as to the use of cortisone or ACTH should become routine.

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### TRANSIENT ELECTROCARDIOGRAPHIC CHANGES SIMULATING AN ACUTE MYOCARDITIS IN SERUM SICKNESS\*

By DAVID H. NEUSTADT, M.D., *New York, N. Y.*

THIS case report describes changes in T wave compatible with an acute myocarditis found in a routine electrocardiogram taken on a young woman with generalized allergic manifestations caused by horse serum. With subsidence of the allergic phenomena two days later, the electrocardiographic abnormalities disappeared.

#### CASE REPORT

A 27 year old white single woman entered the hospital for the first time with generalized urticaria, joint pains and bilateral periorbital edema. Nine days before she had sustained a small puncture wound from a rusty nail which was treated in the Lenox Hill Hospital Emergency Room. An intradermal test with tetanus antitoxin was positive. The following day the skin test was repeated and found to be negative. Accordingly, 10,000 units of tetanus antitoxin were administered subcutaneously. Five days following this injection the patient developed erythematous wheals over her entire body, and three days later she noted ankle edema and swelling around both eyes. A local physician treated her with intravenous Benadryl and calcium gluconate, and adrenalin subcutaneously, without relief. After the adrenalin there was palpitation, and four hours later nausea, weakness, shortness of breath and increased puffiness of her face. More adrenalin was given subcutaneously, as well as Pyribenzamine by mouth, without amelioration of her symptoms. She was admitted to the hospital.

Past history and family history were noncontributory. There was no allergic history, either personal or familial.

The admission physical examination revealed a rectal temperature of 99.8° F., pulse 100, respirations 22, and blood pressure 128/70 mm. of Hg. She weighed 94 pounds. There was a generalized urticarial rash with excoriations, and the patient was in moderate distress from severe pruritus. There was bilateral periorbital puffiness, with minimal injection of pharynx. The heart displayed a normal sinus rhythm. There was no murmur, thrill or friction rub. The sounds were of good quality. There was a trace of ankle edema. There were a few discrete tender axillary nodes.

Initial laboratory data revealed a normal hemogram (hemoglobin 17 gm.; red blood cells, 5.5 million; hematocrit, 50.8, with white blood cell count, 5,900; polys. 63; lymphocytes, 37). The results of other tests were as follows: erythrocyte sedimentation rate (Westergren method), 1.5 mm./30 min.; 3.0 mm./one hour; blood urea nitrogen, 11.8 mg. per 100 ml.; blood glucose, 91.0 mg. per 100 ml. Urine, negative (cloudy; specific gravity, 1.020, with acid reaction; albumin, negative;

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From the Cardiovascular Service, Lenox Hill Hospital, New York, N. Y.

sugar, negative; acetone, negative; microscopic: occasional white blood cells, few epithelial cells and much mucus). Mazzini and Kline tests were negative.

Teleroentgenograms of the chest taken on the second and fourth days of hospitalization were similar and revealed a heart and aorta normal in size and shape. The lungs were clear, without evidence of any active pulmonary disease.

Electrocardiograms were recorded also on the second and fourth hospital days and differed from each other as shown in figures 1 and 2. The significant difference between the two was the ventricular gradient, manifested principally by differences in the T wave. In the first the mean direction of the spatial T vector was upward,

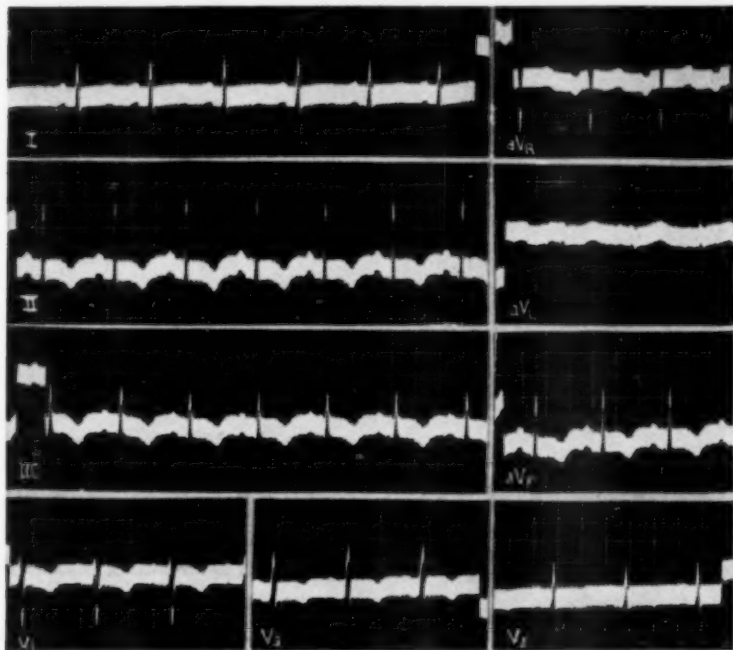


FIG. 1. Standard leads (I, II, III), unipolar extremity leads (aVR, aVL, aVF), and unipolar precordial leads ( $V_1$ ,  $V_2$ ,  $V_3$ ), recorded on second day of hospitalization when patient had urticaria and fever. To be noted: the abnormal T waves. Time lines occur every 0.04 second. Precordial leads one-half normal sensitivity.

backward and to the left, with an angle of  $142^\circ$  between the QRS and T vectors in the frontal plane. In the second record the spatial T vector was directed downward, forward and to the left, and the angle between the QRS and T vectors in the frontal plane was  $36^\circ$ . The auricular and ventricular rates in the two curves were 100 and 62 beats per minute, respectively.

**Course:** The patient was treated with an intramuscular dose of 40 mg. of ACTH. No other therapy save sedation was given. The following day the temperature rose to  $101.4^\circ$  F. and the pulse rate reached 110 per minute. However, there was considerable clearing of the rash, with diminution of itching, and the patient was obviously improved and more comfortable. A second dose of 20 mg. of ACTH was

administered. The area over the sternum became exquisitely tender, although there was no local redness, increased heat, swelling or eruptions on the anterior chest wall at this time. On the following day, when the temperature and pulse rate were within normal limits, the localized area of tenderness over the sternum disappeared. The patient was discharged on the fourth day after admission.

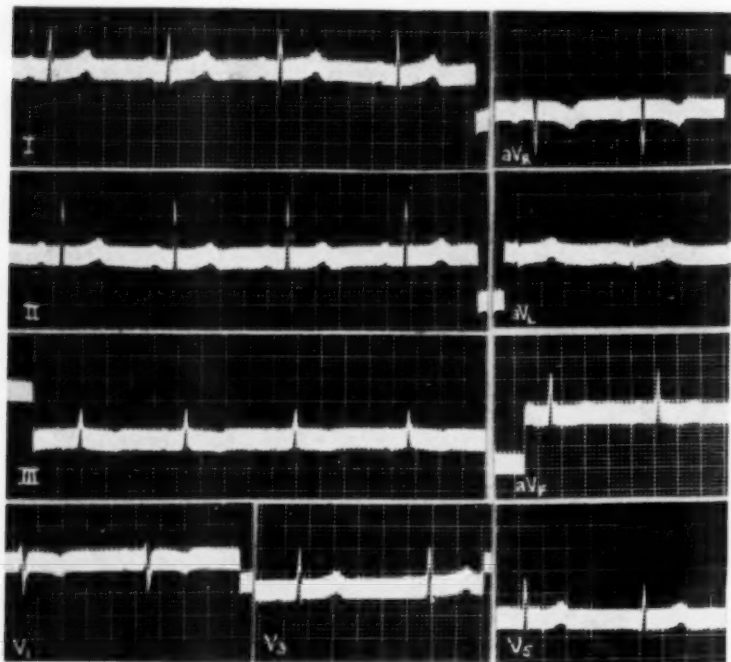


FIG. 2. Electrocardiogram as in figure 1 recorded on fourth day of hospitalization, after all evidence of serum sickness had subsided.

#### DISCUSSION

In the recent literature there have been reported two separate cases of an allergy associated with unusual electrocardiographic changes. Lilienfeld et al.<sup>1</sup> reported a case of sulfonamide sensitivity with electrocardiographic changes including bundle branch block simulating those seen with myocarditis. Foster and Layman<sup>2</sup> discussed a patient with generalized urticaria as a result of drug sensitivity, with electrocardiographic abnormalities suggestive of myocardial infarction, with bundle branch block that disappeared after 12 days.

In the past, attention has been directed to the rôle of allergy in the production of parenchymal lesions of the myocardium. Rudolf Jaffe<sup>3</sup> described experiments with rabbits and guinea pigs which had been sensitized to horse serum or egg white. In these animals pathologic lesions of the myocardium were observed which compared to lesions seen in human myocarditis, though

milder. These results supported similar findings described by earlier workers, i.e., Klinge in 1932,<sup>4</sup> Bruun in 1939,<sup>5</sup> Rich and Gregory,<sup>6</sup> Fox and Jones<sup>7</sup> and Longcope.<sup>8</sup>

Jaffe<sup>9</sup> concluded from the above that human myocarditis may be due to several factors: an unspecific allergy and a toxic or specific allergy. A less severe type of myocarditis was produced experimentally by sensitization of animals to extracts of heart muscles prepared from animals of the same species. By combining specific heart muscle extract and some unspecific allergen or toxin, i.e., horse serum, egg albumin or killed streptococci, a more severe, diffuse myocarditis was produced.

Several instances of myocardial lesions following the introduction of a sensitizing drug have been reported in the literature. Brown and McNamara<sup>10</sup> described a case of acute interstitial myocarditis complicating exfoliative dermatitis due to neoarsphenamine used in the treatment of syphilis. French and Weller,<sup>11</sup> in a routine microscopic examination of autopsy material, found an interstitial myocarditis, rich in eosinophilic cellular infiltrations, in the hearts of 126 patients whose only common factor was that the sulfonamide drugs had been administered shortly before death. They produced similar lesions in mice and rats with the intraperitoneal injection of sulfonamides in amounts even smaller than the comparable human dosage. Wells and Sax<sup>12</sup> have reported a case of isolated myocarditis that followed the administration of sulfadiazine. Goodman<sup>13</sup> described a case apparently due to sulfonamide sensitivity with myocardial involvement in which a skeletal muscle biopsy showed lesions similar to those of periarthritis nodosa.

Several authors have supported the concept of serum carditis in man as described by Clark and Kaplan.<sup>14</sup> They found a proliferation of histiocytes in the mural and valvular endocardium, accompanied by multiplication of the interstitial cells of the myocardium, in two patients who received intravenously large doses of antipneumococcus horse serum and came to necropsy after the development of serum sickness. They suggested that the endocardial and other mesenchymal alterations associated with serum reaction represent the morphologic expression of a hyperergic state associated with serum sickness.

Wadsworth and Brown<sup>15</sup> reported a serum reaction complicated by an acute carditis in an 11 year old boy following injection of 5 ml. of combined tetanus and gas antitoxin in horse serum. In this patient the serum reaction was slightly atypical in that urticaria and joint symptoms were absent. The authors offer the possibilities that the carditis may have originated from the horse serum per se, or that the horse serum may have activated a subclinical rheumatic fever.

Fox and Messeloff<sup>16</sup> reported a case of an 18 year old boy who sustained a typical serum reaction following administration of tetanus antitoxin, similar in nature to the present case. They described serial electrocardiographic abnormalities taking the form of definite lowering of QRS in the standard leads and a slight elevation of the ST segments in Leads II and III. The tracings showed a gradual increase in the voltage of the ventricular complex, with a return to normal nine days after admission, when the patient had fully recovered. The electrocardiographic alterations were attributed to the structural changes in the heart as described by Clark and Kaplan, above.

One other interesting case, described by McKinley,<sup>17</sup> is that of a 21 year old white male who had received a prophylactic injection of tetanus antitoxin with subsequent occurrence of serum sickness, in which marked cardiac enlargement, pericarditis and pleurisy ensued. After a course of 58 days the disease abated abruptly. Serial electrocardiograms revealed tracings consistent with pericarditis, with return toward normal at the termination of the illness.

In the present case there is a possibility that the electrocardiographic abnormalities observed could have been caused by the drugs received. Since such abnormalities have not been observed after epinephrine in clinical dosage, after ACTH, or after antihistaminics, this possibility seems remote.

#### SUMMARY

1. A case is reported of serum sickness in a young woman following the administration of tetanus antitoxin.

2. A routine electrocardiogram demonstrated T wave alterations compatible with an acute myocarditis.

3. T wave abnormalities disappeared and a complete resolution of signs and symptoms occurred two days later, following the intramuscular administration of ACTH in two daily doses of 40 and 20 mg., respectively.

#### ACKNOWLEDGMENT

The author is grateful to Dr. Charles E. Kossmann for his help in the preparation of this report.

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### HYPERVITAMINOSIS A: REPORT OF A CASE IN AN ADULT MALE \*

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THE syndrome of hypervitaminosis A has been described in at least 17 infants and young children since Josephs' original article in 1944.<sup>1,2</sup> Sulzberger and Lazar<sup>3</sup> described similar toxic symptoms which occurred in an adult female who took large amounts of vitamin A in an attempt to prevent colds. Rodahl<sup>4</sup> has described the toxic symptoms of hypervitaminosis A resulting from polar bear liver ingestion.

The present report is of an adult male with this syndrome and demonstrates several interesting features.

#### CASE REPORT

*Present Illness:* A 25 year old Mexican drug store clerk was first seen by us on March 3, 1952. He complained of marked asthenia, a 10 pound weight loss, anorexia, polydipsia, polyuria, a skin rash, excessive loss of the hair of the entire body, soreness and fissuring of the lips, and pain in the area of the shoulder joints, ribs, tibia and ankles. All of his symptoms were of about two weeks' duration. He and his family believed that he was very seriously ill.

Questioning revealed that for about two months the patient had been taking three to four vitamin A capsules daily (50,000 U.S.P. or international units per capsule), and two to three multivitamin capsules daily, each of which contained 25,000 units of vitamin A. He had also taken three ampuls of vitamin C and four or five 1 mm. injections of liver during that period. The patient would often omit a meal and take vitamin capsules in lieu of eating. Shortly after the onset of the above symptoms the patient was seen by a physician in Tijuana, Mexico, who prescribed three injections of cortisone, three ampuls of 2 ml. each of vitamin B complex, and three injections of a sodium salicylate-colchicine, sodium iodide preparation. The patient discontinued vitamin A and all other medications about one week before entering the hospital.

*Past History:* The patient had been in good health and had had no previous serious illness. He had never had any known liver disorder. Family history was noncontributory.

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*Physical Examination:* The patient was a well developed, alert, coöperative white male looking his stated age of 25. He appeared acutely ill. The significant findings were the following:

1. A patchy alopecia. The hair of the scalp or any part of the body could be pulled out with ease. The patient's pillow-slip and bed linen were always littered with his hair. There were oval areas of alopecia on the legs.
2. A maculopapular rash on the chest, oiliness of the skin on all areas of the body, desquamation of the skin over both heels, and a strong odor emanating from the skin.
3. Slight faucial injection and marked desquamation of the buccal mucous membrane.
4. A sinus tachycardia (rate 100 to 110), though the blood pressure, heart size and sounds were normal.
5. Liver enlarged by palpation three fingerbreadths below the right costal margin, nontender.
6. Marked tenderness over many bones, particularly the left clavicle, the lower ribs and both tibiae.

*Laboratory Studies:* *March 3, 1952:* Complete blood count, normal. Fasting blood glucose, 110 mg. per cent. *March 5, 1952:* Red blood count, 3.97 million. Hemoglobin, 12 gm., 84 per cent. White blood count and differential, normal. Total proteins, 7.0 gm. Serum albumin, 3.81 gm. Serum globulin, 3.19 gm. Cholesterol (total), 162. Alkaline phosphatase, 7.0 units. Bromsulfalein, 1.5 per cent retention in 45 minutes. Icterus index, 16. Cephalin flocculation, 1 plus in 48 hours. Bilirubin, 1.6 mg. per cent. Calcium, 13.6 mg. per cent (normal, 9 to 11.5). Phosphorus, 3.1 mg. per cent. Kline and Kahn, negative. *March 10, 1952:* Blood prothrombin time, 14 seconds (control, 17 seconds); concentration, 156 per cent. Blood carotenoids, 23 micrograms per cent (normal, 100 to 225). Blood vitamin A alcohol, 183 micrograms per cent (normal, 20 to 60). *March 18, 1952:* Blood carotenoids, 82 micrograms per cent. Blood vitamin A alcohol, 237 micrograms per cent. Serum calcium, 12.7. *March 28, 1952:* Blood carotenoids, 69 micrograms per cent. Vitamin A alcohol, 153 micrograms per cent. Urine: *March 3, 1952:* Routine urinalysis, normal. *March 5, 1952:* Bence-Jones protein determination, negative. *March 8, 1952:* Sulkowitch test, "milky reaction" (strongly positive). *March 10, 1952:* Sulkowitch test, normal. *March 18, 1952:* Sulkowitch test, normal.

*X-Rays (March 3, 1952):* X-rays of the chest, abdomen and skull were completely normal. There was no evidence of osteoporosis or cortical hyperostosis. *Electrocardiogram (March 3, 1952):* Normal except for slight tachycardia (rate, 104).

*Course:* The patient received no therapy other than withdrawal of vitamin A and modified bed-rest. He was advised to restrict the intake of butter and cream. The symptomatic improvement was rapid. Two days after he entered the hospital the bone and joint pain disappeared, the appetite returned to normal, and the asthenia was replaced by a sense of well being. The skin rash and the desquamation of the buccal mucous membranes cleared rapidly. The hair continued to fall out and to be coarse and brittle for about three weeks, then it began to grow back and to lose its brittleness. Much of the hair of the eyebrows and eyelashes fell out about two weeks after he entered the hospital.

The liver enlargement decreased gradually. Two weeks after his entry into the hospital the liver was palpable two fingerbreadths below the right costal margin; three weeks after entry it was one fingerbreadth below the right costal margin.

The pulse rate returned to normal about three days after his admission to the hospital.

The patient was discharged eight days after entry into the hospital and continued to convalesce at home. He rapidly regained the lost weight. About two months after the onset of his symptoms he was clinically well.

#### DISCUSSION

The essential differences in this case from the similar case in an adult female previously reported are that our patient did not present pruritus, skin pigmentation, exophthalmos or sexual alterations, but did demonstrate hepatomegaly and a greasy odorous skin. Features presented common to cases previously reported in infants and children included bone and joint pain, skin rash, alteration of the mucous membranes of the lips, asthenia, weight loss, anorexia and hepatomegaly.

Factors other than the mere ingestion of large amounts of vitamin A may be involved in the pathogenesis of this condition. Josephs,<sup>1</sup> for example, cited the observation of an eight month old infant who received 500,000 units of vitamin A daily over a period of four months, with no symptoms of toxicity and with a normal blood vitamin A level. All authors have reported complete recovery from this syndrome following withdrawal of vitamin A. Several have repeated experimentally the clinical syndrome after the symptoms had subsided by re-administering high doses of vitamin A.

Rodahl<sup>2</sup> in excellent monographs has reviewed the subject of the toxic effect of polar bear liver and hypervitaminosis A, and has contributed interesting observations on experimental animals. He states that it has been known for centuries among Eskimos and Arctic travelers that the ingestion of polar bear liver by men or dogs causes severe illness. Acute symptoms of severe headache, dizziness, irritability, vomiting and diarrhea occur following the ingestion of polar bear liver. After about a week or more, peeling of the skin and some loss of hair may occur. Rodahl demonstrated by feeding experiments with rats that the large amounts of vitamin A in polar bear liver were responsible for these toxic symptoms.

#### CONCLUSION

A case of hypervitaminosis A in an adult male is reported. The patient presented anorexia, weight loss, asthenia, skin rash, loss of hair, polydipsia, polyuria, soreness and fissuring of the lips, bone and joint pain, hepatomegaly and tachycardia. He made a prompt recovery following cessation of vitamin A ingestion. The similarities and differences between this case and the others reported are discussed.

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### ACUTE *LEPTOSPIRA POMONA* ARTHRITIS AND MYOCARDITIS\*

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A case is reported below of acute arthritis and myocarditis associated with specific serologic reactions of leptospirosis due to *Leptospira pomona*, which resembled rheumatic fever sufficiently closely to require specific diagnostic methods for differentiation. The case presented symptomatology not heretofore described in leptospirosis, and increased the number of clinical pictures that suggest the possibility of leptospiral etiology.

The leptospiroses are a group of illnesses caused by spirochetes of a number of immunologically distinct strains. *Leptospira icterohaemorrhagiae*, the cause of Weil's disease, and *Leptospira canicola*, the cause of canicola fever, were comparatively well known in the United States before 1951. Evidence of human infection with *Leptospira pomona* was first recognized in the United States in 1951.<sup>1</sup> Reports of other cases of *L. pomona* infection soon followed,<sup>2</sup> as well as reports of cases of infection with other strains, namely, *Leptospira autumnalis*,<sup>3</sup> and *Leptospira grippotyphosa*.<sup>4</sup> Fourteen different specific leptospires were recognized by Gsell<sup>5</sup> as a result of studies of the strains of leptospires and reports of cases and epidemics of illness from all parts of the world. The infections caused two main groups of clinical manifestations. The first group comprised infections that were sometimes severe and often associated with jaundice. They

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were caused by *L. icterohaemorrhagiae*, *L. bataviae*, *L. autumnalis*, *L. pyogenes*, *L. andaman* A, or *L. bovis*. The second group of infections were usually mild and were often associated with aseptic meningitis. These infections were caused by *L. grippotyphosa*, *L. hebdomidis*, *L. sejroe*, *L. saxkoebing*, *L. australis* A, *L. pomona*, *L. mitis* and *L. canicola*. The etiologic agent in the present case was classified by Gsell<sup>5</sup> with the latter group.

Both joint pains and clinical manifestations of myocardial damage were described as minor features of leptospirosis. Gsell<sup>5</sup> stated in a review that pains in the muscles, most marked in the lower extremities, were common in various types of leptospirosis, but that joint symptoms were rare. Two specific reports of joint pains were found in the literature. Nielsen and Hertel<sup>6</sup> found myalgias present in 17 cases (or 58 per cent) of their series of *L. sejroe*, but in three cases both knees and the adjacent calf muscles were involved. Gsell<sup>5</sup> reported a case of *L. sejroe* infection with tonsillitis and rheumatic pains, but he considered the latter symptoms probably due to an associated unrelated infection. Gsell<sup>5</sup> also reported that the incidence and severity of myocardial damage in leptospirosis were similar to those in other infectious diseases, chiefly bradycardia, hypotony and disturbances of rhythm. Bertucci<sup>7</sup> in a review, referring only to Weil's disease caused by *L. icterohaemorrhagiae*, listed occasional dilatation of the heart and hemic murmurs, but more commonly gallop rhythm, premature extrasystoles, auricular flutter and fibrillation, and pericardial friction rubs. He also stated that the electrocardiogram occasionally showed prolonged QT and PR intervals, defective AV conduction, functional or real incomplete AV blocks, low T waves, blocked auricular beats, sinus tachycardia and low voltage QRS complexes. These changes were nearly always reversible with convalescence.

Nielsen and Hertel<sup>6</sup> described two cases that showed cardiac symptoms of 27 with *L. sejroe* infection. One, a woman with hyperthyroidism, developed auricular fibrillation. Another woman complained of precordial oppression, and had many extrasystoles and a flat T wave in Lead II of the electrocardiogram. Both returned to normal promptly when fever disappeared. The following four cases, two with microscopic evidence of myocarditis and two with endocardial involvement, were reported to have pathologic evidence of cardiac lesions that were thought to be of clinical significance. Kaneko (reported by Drägers<sup>8</sup>) recorded one case of severe myocarditis seen at post mortem following Weil's disease. Ashe, Pratt-Thomas and Kumpe<sup>9</sup> found microscopic evidence of myocarditis at post mortem in one of their cases of Weil's disease. Drägers<sup>8</sup> found endocarditis with nodular lesions at post mortem in two cases of Weil's disease, and in one of these spirochetes were demonstrated in microscopic sections of the heart valve.

#### CASE REPORT

The patient, a 37 year old white male, was a distributor for an oil company and lived in a town of about 12,000 population in Mississippi. He was admitted on April 23, 1952, complaining of an illness of one week's duration, beginning with an episode of paroxysmal coughing which was nonproductive and had no relation to exertion. On the following day while he was playing baseball his left ankle became painful and swollen. During the day he developed fever and malaise, and during the succeeding week a migratory type of joint pain involving the knees, ankles, wrists and shoulders. Swelling was absent except for that of the left ankle, which persisted to admission.

Four days before admission he was treated by his physician for pharyngitis. He developed chills and, two days before admission, a bandlike headache and nausea and vomiting. Bilateral anterior chest pain aggravated by deep breathing and coughing appeared. He complained of some difficulty in initiating urination throughout the present illness.

His past history showed no significant previous illnesses. He lived in town and had little contact with farm animals except that two months before admission he transported two small pigs in the trunk carrier of his passenger car to a farm. These pigs were well and still living at the time of the patient's admission. Reference will be made later to agglutination reactions of serum specimens from these pigs.

**Physical Examination:** The patient was a short, stocky white male with flushed face, a mild conjunctival injection, swelling of the eyelids, and a generalized patchy erythema of the upper trunk which blanched on pressure. His temperature was 102° F.; his pulse rate was 120 beats per minute, and his blood pressure was 118/70 mm. of mercury. His respirations were shallow, rather rapid and labored. Fine inspiratory moist râles were audible at both lung bases posteriorly. Obesity prevented definite estimation of cardiac border. The rhythm was regular and no adventitious sounds were heard. There was some mild tenderness in the subxiphoid region. The liver and spleen were not palpable. One soft, tender supraepitrochlear lymph node was felt on the right. The left ankle was swollen, warm and tender. Both knees were tender at the joints but without swelling. The prostate was slightly enlarged and tender and felt soft.

**Laboratory Data:** The white blood count was 9,900 leukocytes per cubic millimeter of blood. The differential count showed 85 per cent polymorphonuclear leukocytes. The sedimentation rate was 32 mm. per hour (Westergren method). The red blood cell count was 4,100,000 cells per cubic millimeter of blood, and the hemoglobin estimation was 12.5 gm. per cent. The urine was negative. A blood culture taken on admission, serologic tests for syphilis, blood CO<sub>2</sub> and chlorides, serum bilirubin and thymol turbidity were all normal. Agglutination tests with typhoid O, typhoid H, paratyphoid A, paratyphoid B, and *Proteus* OX19 were negative on the eighth day of illness. Agglutination tests for brucellosis and tularemia were negative on the sixteenth and twenty-sixth days of illness. Cold agglutinins were absent on the sixteenth day but present when serum obtained on the twenty-sixth day of illness was diluted 1:16. Antistreptolysin titers on the eighth, thirty-fifth and forty-ninth days of illness were normal.

Cultures and a technic furnished by Dr. Martha K. Ward were employed in serologic agglutination tests performed with *L. icterohaemorrhagiae*, *L. canicola* and *L. pomona*. Tests on admission (the eighth day of disease) were negative with all three antigens and remained negative with *L. icterohaemorrhagiae* throughout the illness. Positive *L. pomona* agglutination tests were given by serums obtained on the fourteenth and twenty-first days of illness when the serums were diluted 1:4,096. The titers of subsequent serums declined, being 1,024 on the thirty-fifth day, 256 on the forty-second and forty-ninth days, and negative on the ninety-ninth day after onset. Weak cross-agglutinations were obtained with *L. canicola* for three weeks during the height of the infection, the titer never rising above 16.

The electrocardiogram on admission was interpreted as being within normal limits, but changes indicating the presence initially of pericarditis or myocarditis appeared in later tracings and again returned to normal at the time of discharge (figure 1). The chest roentgenogram on admission showed cardiac enlargement, increased bronchovascular markings, and an infiltration in the right lower lung field (figure 2). Four days later, platelike atelectasis was seen in the right midlung field. The heart was further enlarged, and congestive changes were noted bilaterally. On

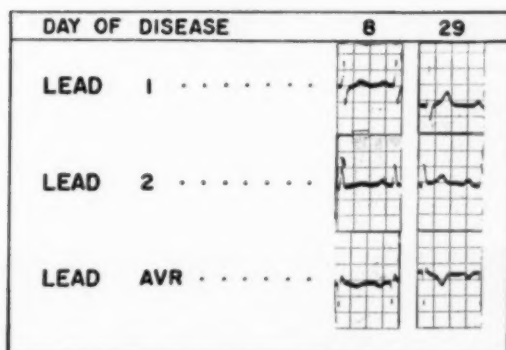


FIG. 1. Electrocardiographic tracing on admission (eighth day) and on the twenty-ninth day of disease, showing evidence of myocardial damage and return to normal.

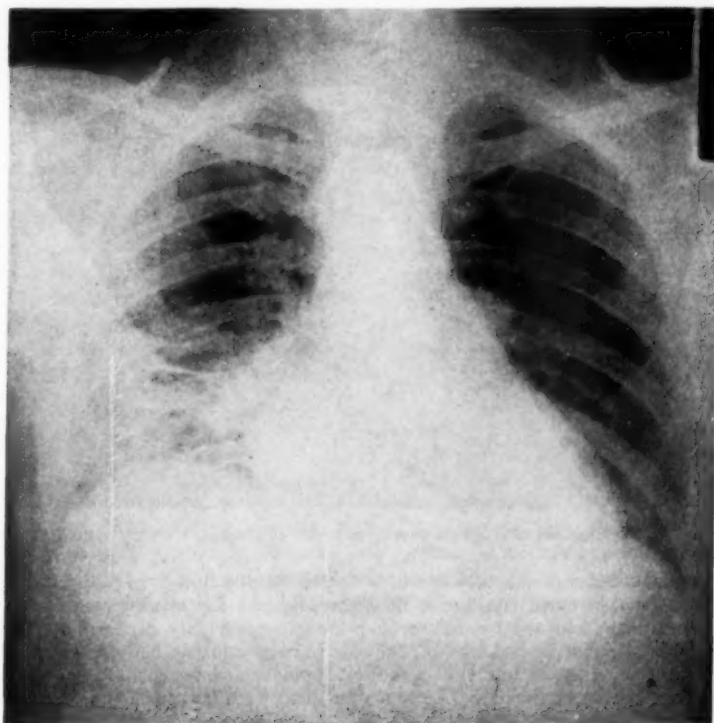


FIG. 2. Roentgenogram of chest on admission (eighth day of disease), showing pulmonary congestion, infiltration and enlarged cardiac silhouette.

the twenty-first day of the disease both lung fields were clear and the heart had returned to normal size (figure 3).

**Hospital Course:** The patient's respiratory distress was severe and anterior chest pain was persistent. Three days of treatment with terramycin, beginning on the eighth day of illness, resulted in no clinical improvement, but when salicylates were begun on the tenth day of illness, symptoms were relieved within 24 hours and temperature returned gradually to normal in 48 hours. Joint pains disappeared except for a reappearance of mild left shoulder pain for three more days. The sedimentation rate remained elevated from 32 to 37 mm. per hour (Westergren method) until

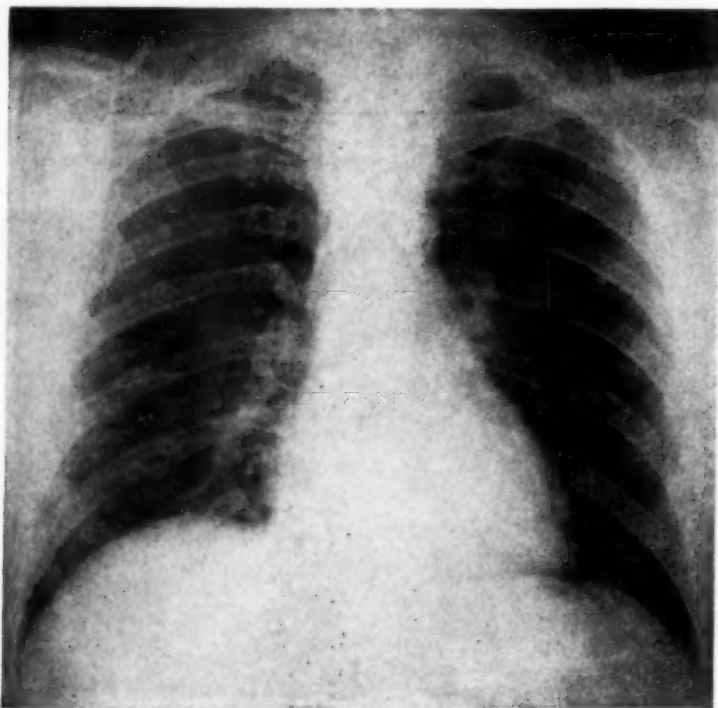


FIG. 3. Roentgenogram of chest on twenty-first day of disease, showing return to normal.

the twenty-sixth day of illness, when it decreased steadily to normal at discharge. He was discharged as cured on June 5, 1952, the fifty-first day after onset of his illness.

The patient returned for follow-up examination on July 21, 96 days after the onset, reporting that he had worked daily in an office and had had occasional pain in both ankles, more in the left, and in the left shoulder and occasionally in both knees. He had gained approximately 22 pounds and had no other complaints except for a general lack of strength.

He furnished serums from the two pigs mentioned above, which he stated were still living and well. These serums failed to agglutinate *L. icterohaemorrhagiae* or *L. canicola*, but agglutinated *L. pomona* when diluted to 1:128 and 1:256, respectively.

## DISCUSSION

The symptomatology of this case was unusual when compared with typical leptospirosis, in that joint pains with obvious swelling and redness of one joint, precordial distress, enlargement of the cardiac shadow, the electrocardiographic changes of myocarditis, and pulmonary congestion and respiratory distress dominated the picture. Headache was present and vomiting occurred before hospital admission, indicating the possibility that a meningeal reaction occurred. The spinal fluid was not examined, however, because there were no physical signs of meningeal involvement, and the results of specific agglutinations became known late in the disease when the patient had completely recovered. Conjunctival injection and patchy erythema on the trunk were observed on admission, but their significance was diminished by the clinical course of the illness.

The patient's story of migrating joint pains was accepted and a tentative diagnosis of rheumatic fever was made. The response to salicylate therapy was striking, and it further substantiated the initial impression. Daily cardiac auscultation early in the illness and later, when pulmonary congestion had cleared, failed to reveal any cardiac murmur or friction sound. The age of the patient and the severity of the cardiac involvement without evidence of previous rheumatic disease led to a search for other etiology. Because of the first clinical impression on admission, based upon the observation of marked conjunctivitis with swelling of the eyelids, and the report of a bandlike headache and vomiting before admission, the possibility of leptospirosis was considered throughout the course of the illness and sera were collected for specific agglutination tests. Serologic agglutination tests were pathognomonic of *L. pomona* infection. The antistreptolysin titers were normal and made the diagnosis of concurrent rheumatic fever in retrospect very unlikely.

Only one possible source of infection from pigs was found but the animals were well, the amount of exposure was slight, and the contact had occurred two months before the onset of the patient's illness. The presence of specific agglutinins in the sera of the animals was also of some interest but did not show positively that the animals were carriers of *L. pomona*. The source of infection was therefore not completely established, but suspicion attaches to the carrying of the animals in a closed automobile driven by the patient.

This case suggests the possibility that certain cases of leptospirosis may be considered to have acute rheumatic fever because of their symptomatology. This problem in differential diagnosis was pointed out by Gsell<sup>8</sup> in the most comprehensive available review of the subject, but without illustrative cases. It seems probable that little difficulty will ordinarily be met in differentiating the two conditions when the distinctive features of leptospirosis are kept in mind, such as conjunctivitis, the predominance of muscular pains rather than joint pains in the average case of the disease, and the symptoms of aseptic meningitis. Also, it should be noted from this experience that leptospiral disease, other than Weil's disease, can produce a rather severe course, with cardiac involvement of a marked degree. Only further experience will show the frequency of cases in which the resemblance to rheumatic fever associated with a satisfactory response to salicylates might lead to the diagnosis of rheumatic fever. In general, it can be stated that the recognition of leptospirosis in the United States may

be lagging behind the actual occurrence of the disease because of a too narrow conception of the clinical manifestations, and a too narrow conception of the number of immunologically distinct strains of leptospira. Appropriate agglutination and culture methods in atypical cases of acute infection may disclose other new syndromes due to various strains of leptospirae.

#### CONCLUSIONS

A case is described of *Leptospira pomona* infection which resembled rheumatic fever and was associated with an unusual degree of acute myocardial involvement. The differential diagnosis of rheumatic fever and leptospirosis is discussed.

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#### ASPIRATION PNEUMONITIS COMPLICATING POLIOMYELITIS: A CASE SUCCESSFULLY TREATED BY EXSUFFLATION \*

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THE purpose of this report is to describe the clinical course of a patient with spinal poliomyelitis who developed pneumonitis and pulmonary atelectasis sec-

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† With the technical assistance of Mr. FRED DRIMMER.

ondary to the aspiration of gastric contents. The physiologic and therapeutic effects achieved by the use of the Exsufflator in this condition will be presented.

The incidence of atelectasis and aspiration pneumonitis in bulbospinal poliomyelitis patients has been estimated at about 25 per cent, and in 80 per cent or more of these patients death is due to these pulmonary complications.<sup>1,2</sup> The urgency of improving impaired ventilatory function by removal of obstructing mucous plugs from the bronchi of patients with ineffective cough is apparent from these facts.

This need for mechanical assistance in the expulsion of obstructing mucus stimulated the development of two physical methods which would imitate the natural cough: the cough chamber and the Exsufflator.<sup>3-7</sup> The latter device was used in this study because of its simplicity and ease of transportation.

In the Exsufflator method,<sup>5</sup> inflation of the lungs is accomplished by the pull, over a two-second period, of a negative pressure of 40 mm. Hg, produced by a vacuum-cleaner motor in a conventional tank respirator. When the peak pressure is reached, a butterfly-valve five inches in diameter opens the tank to the atmosphere, releasing the first three-quarters of the negative intratank pressure in 0.03 to 0.04 second. This abrupt pressure rise causes a swift recoil of the lung from its initial inspiratory expansion to the expiratory position, resulting in expulsion of the alveolar air to the mouth at a high volume flow rate. During the maximal dilatation of the bronchi in the inspiratory phase, air flows past the obstructing plugs of mucus to the alveoli. In the expiratory phase, when the bronchi are narrowed, the increased pressure of the air trapped behind the plugs tends to expel them toward the mouth.<sup>6</sup> At the moment of the termination of negative pressure, the patient is propelled toward the head end of the respirator and then suddenly stopped by the collar baffle, effecting simultaneously, a headward movement of secretions and an impact on the diaphragm by the viscera through the operation of inertia.

#### CASE REPORT

A 21-year-old nurse was admitted to Grasslands Hospital on August 18, 1952, complaining of dysphagia and nuchal rigidity following an upper respiratory infection of six days' duration. Pains in the lower extremities, malaise, generalized weakness and postprandial vomiting had occurred during the last three days.

She had had a previous admission to Grasslands Hospital (in August, 1950) for nonparalytic spinal poliomyelitis, a diagnosis confirmed by cerebrospinal fluid tests, physical findings and clinical course.

Temperature on the present admission was 103° F.; pulse rate, 128 per minute; blood pressure, 170/110 mm. Hg. The pharynx was inflamed and filled with frothy sputum. The gag reflex responded slowly and fatigued rapidly. The Kernig and Brudzinski signs were positive. Of 84 white blood cells found in the spinal fluid, 49 were mononuclear and 35 polymorphonuclear cells. The Pandy protein reaction was 2 plus, the total proteins being 118 mg. per cent; sodium chloride content, 730 mg. per cent; and the complement-fixation reaction for syphilis, negative. Cultures of nose and throat washings revealed *Staphylococcus albus*, *Neisseria catarrhalis*, *Streptococcus viridans* and a nonhemolytic streptococcus. The CO<sub>2</sub> combining power was 64 vol. per cent. The white blood count was 10,300, with 74 per cent polymorphonuclear leukocytes and 26 per cent lymphocytes. For three days after admission the temperature remained elevated, and difficulty in swallowing increased progressively. Muscle examination revealed weakness of the sternocleidomastoid and triceps muscles bilaterally, and of the right biceps, deltoid and pectoral muscles. Phrenic

nerve involvement was suggested by diaphragmatic weakness, with poor cough and inability to contract during sniffing. During the early course of treatment, oropharyngeal secretions were drained by placing the patient in the head-down position, and by the frequent use of suction. Nutrition and hydration were maintained by gavage. On the fourth and fifth days there was progressive decrease in vital capacity from 1,400 to 1,200 c.c. (figure 1). Bilateral facial weakness and total palatal weakness developed. On the sixth day, diminution of the patient's voice and right deviation of the tongue became evident, and the  $\text{CO}_2$  combining power rose from 66 per cent to 71 per cent in 24 hours. On the morning of the sixth day, the patient vomited gastric contents, part of which she aspirated.

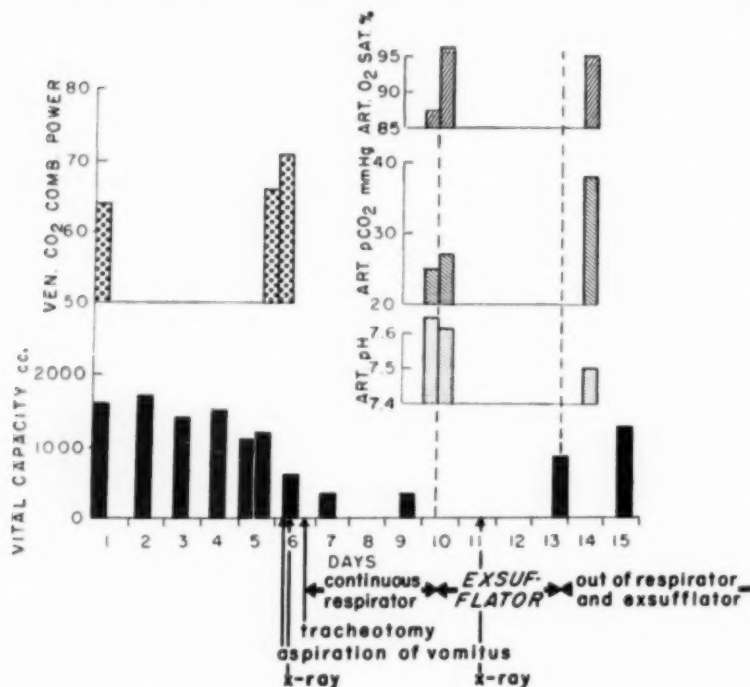


FIG. 1. Correlation of clinical and laboratory data throughout the course of M. J. N. A rapid diminution in vital capacity from 1,200 c.c. to 350 c.c. followed the aspiration of vomitus on the sixth hospital day. Tracheotomy and five days of continuous respirator therapy resulted in hyperventilation, with a fall in  $\text{pCO}_2$  to 24 mm. Hg and an arterial oxygen saturation of 87.4 per cent. Immediately following 30 minutes of exsufflation, a 9.1 per cent rise of oxygen saturation to 96.5 per cent took place, without significant change in pH or  $\text{pCO}_2$ . Four days after initiation of exsufflation, vital capacity increased to 850 c.c., and removal from the respirator and Exsufflator was possible, with good oxygenation and normal  $\text{pCO}_2$  and pH of the arterial blood.

Slight cyanosis of the lips and nail-beds then became apparent, and respirations were irregular. Examination of the chest revealed diminution of breath sounds over the entire right chest, with scattered moist râles present on deep inspiration. Fluoroscopy showed complete paralysis of the right diaphragm. Chest x-ray demon-

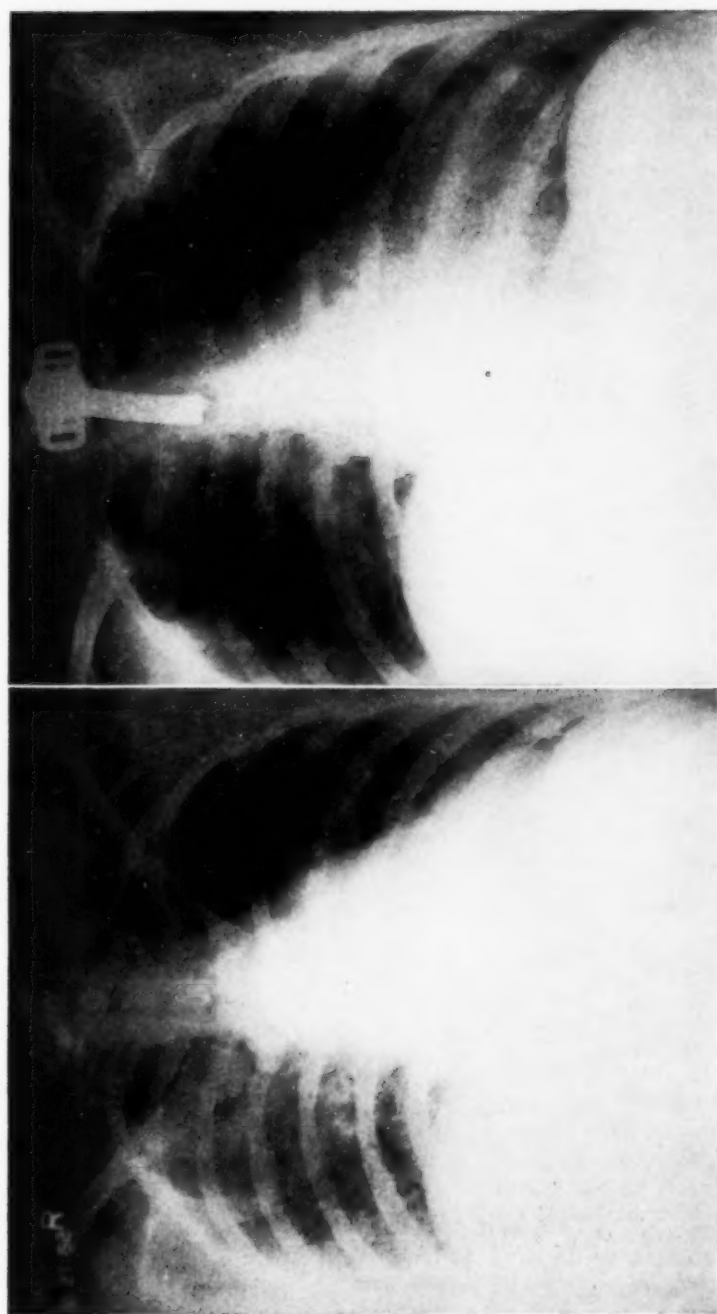


FIG. 2. A. X-ray on day of aspiration of vomitus. Shows infiltration throughout the entire right and the left central lung fields. B. X-ray 24 hours after initiation of exsufflation reveals clearing of the exudative infiltration.

strated infiltration throughout the entire right and the left central lung fields (figure 2A). Temperature reached 105.2° F.

After a tracheotomy, the patient was placed in a tank respirator set for a negative inspiratory intratank pressure of 15 cm. H<sub>2</sub>O and a positive expiratory intratank pressure of 6 cm. H<sub>2</sub>O at a rate of 20 per minute. She received 400,000 units of penicillin and 1 gm. of streptomycin twice daily by intramuscular injection. During the following four days the patient remained in the respirator continuously, with no change in the physical findings. By the fourth day, vital capacity had fallen to 350 c.c.

On the sixth day after the onset of the aspiration pneumonitis and atelectasis, the patient was transferred to the Exsufflator and "coughed" six times a minute for 15 minutes of each hour during the day and twice at night, using a negative inspiratory intratank rise to atmospheric pressure in 0.04 second.

Arterial blood studies made while she was in the respirator (figure 1) revealed an oxygen saturation of 87.4 per cent, a pCO<sub>2</sub> of 24 mm. Hg and pH of 7.64. Although no appreciable change occurred in pH and pCO<sub>2</sub>, after the first two 15-minute treatments in the Exsufflator there was a 9.1 per cent rise in oxygen saturation to 96.5 per cent.

Auscultation of the chest immediately after exsufflation revealed increased breath sounds throughout both lung fields. During and after the first day of exsufflation, large amounts of mucopurulent sputum were aspirated from the tracheotomy tube, and after the first 24 hours there was marked reduction in dyspnea and cyanosis. Chest x-rays then revealed clearing of the exudative infiltration (figure 2B).

The Exsufflator was used for 15 minutes of every hour during the day for three more days, with gradual diminution of the mucopurulent secretions which, on culture, manifested growths of *Proteus vulgaris*, *Escherichia coli*, *Staphylococcus albus*, *Streptococcus viridans* and nonhemolytic alpha-streptococcus. After three days of therapy, vital capacity had increased from the 350 c.c. recorded exsufflation to 850 c.c. The patient was comfortable without the respirator for two hours at a time. The arterial pCO<sub>2</sub> rose to 38 mm. Hg and the pH fell to 7.52 within 24 hours of cessation of exsufflation and respirator therapy. At that time the arterial oxygen saturation was 94.6 per cent.

Five weeks after admission the patient became ambulatory. She had residual vocal cord weakness and, although still unable to swallow fluids by mouth, she was able to expectorate her secretion from the oropharynx. The tracheotomy tube was plugged and the patient experienced no respiratory difficulty. She was aphonic, and laryngoscopy on November 14 revealed complete bilateral vocal cord paralysis. Nutrition and hydration were still maintained by gavage.

#### DISCUSSION

The importance of effective coughing to rid the bronchial tree of foreign and infective material is widely and frequently underestimated. Emphasis in the treatment of coughing has been, in many patients, directed toward the use of suppressant drugs rather than toward stimulation of this natural protective mechanism of the human body. The serious complications of inadequate coughing in the presence of obstructed airways have increased our awareness of the necessity for implementing and assisting this defensive mechanism.<sup>1,2</sup> Traditional means of supplementing the natural cough, such as frequent turning during the postoperative period of the convalescing patient, pounding of the thorax to relieve atelectasis, the head-down position for drainage of intrabronchial pus in bronchiectasis, the use of ipecac to induce emptying of the tracheobronchial tree through paroxysmal contraction and release of the diaphragm during vomit-

ing, and bronchoscopy, frequently fail to relieve patients with atelectasis and aspiration pneumonitis.

In 1950, two types of device were developed to imitate by two different methods the physiologic effects of coughing. Since publication of the first report, describing the mechanical cough chamber and the Exsufflator, 13 cases of pulmonary atelectasis, and 35 cases of partial bronchial airway obstruction by mucous plugs,\* have been treated with complete relief within one to five days.

Although bronchoscopy was not performed in the case reported here, this procedure had failed to relieve airway obstruction in seven other cases prior to their treatment by "mechanical coughing," and the case is thus representative of the group of patients treated. The promptness with which this patient could be removed from the respirator after cessation of exsufflation has been duplicated in all cases treated thus far.

X-ray changes presented here are also representative of the other cases treated in the Exsufflator for pulmonary atelectasis and bronchial obstruction (figure 2).

Cherniack and Gordon<sup>6</sup> have described a marked rise in arterial oxygen content and saturation when exsufflation was used during obstructed breathing caused by respiration through a 3 mm. orifice. The same marked improvement in oxygen content observed in this patient after one-half hour of exsufflation has been found in other patients with atelectasis, as well as in those with obstructive emphysema.

The rise in vital capacity indicates rapid improvement of the patient's lung function. Such improvement, in lesser degree than that observed in this case, has also been observed after exsufflation of patients with severe respiratory insufficiency due to residual muscle paralysis following poliomyelitis uncomplicated by airway obstruction. This has been ascribed to the encouragement of increased thoracic excursion by the pull around the chest of 40 mm. Hg negative pressure, the equivalent of 40 mm. Hg positive pressure breathing at the mouth. During exsufflation, the inspiratory volume in paralyzed patients far exceeds individual inspiratory reserve and even vital capacity. Expiratory volume flow rates in the Exsufflator are also much greater than those achieved by the patient's most vigorous self-initiated "cough."<sup>6</sup> This was demonstrated clinically in the reported patient by holding the palm of her hand about three inches above her opened mouth and comparing the relative impact of the exhaled air on the patient's active effort at coughing and on exsufflation. The latter impact proved much more forceful.

In an earlier publication on mechanical coughing,<sup>5</sup> evidence was presented that the hemodynamic effect of exsufflation (compensatory venous pressure rise), with a negative intratank pressure of 40 mm. Hg six times per minute, was less than that of conventional tank respirator treatment with intratank pressure of -20 cm. H<sub>2</sub>O, 20 times per minute.

The head-down position at an angle of 16 degrees was used during exsufflation for two reasons: first, drainage toward the oropharynx was promoted thereby; second, the expulsion of purulent sputum and foreign particles was facilitated by the headward impact of the viscera against the diaphragm during the expiratory phase. Since assistance by manual compression of the diaphragm and the lower ribs has resulted in higher expiratory flow rates than exsufflation

\* A first series of such cases is described in reference 7.

alone, and hence in more rapid clinical improvement, the procedure was used with this patient.

#### SUMMARY

Exsufflation, a procedure designed to imitate some of the physiologic effects of the natural cough, was used in a case of poliomyelitis with aspiration pneumonia due to aspiration of vomitus. A negative tank-respirator pressure of 40 mm. Hg induced inspiration; a swift return of the chest to the expiratory position was produced by a rise of intratank pressure to atmospheric pressure in 0.04 second. A cycling rate of six times per minute was used.

Clinical and roentgenographic changes indicated clearing of the lung lesion after 24 hours of exsufflation. A 9.1 per cent rise in oxygen saturation (from 87.4 to 96.5 per cent) took place within one-half hour of initiation of exsufflation. The elimination of bronchial secretions in this case by exsufflation was similar to the effect produced in 48 other patients in whom mucus or mucopurulent exudate had produced varying degrees of obstruction of the tracheobronchial tree.

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#### CAT SCRATCH ENCEPHALITIS\*

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THERE have been only a few reports of the neurologic manifestations of cat scratch disease. The first published case of encephalitis associated with cat scratch disease was made by Stevens.<sup>1</sup> In this instance the diagnosis was made in retrospect more than two and a half years after the acute illness, by means

\* Received for publication March 10, 1953.

of a skin test with the antigen. Robert Debré et al. have reported convulsive seizures, respiratory paralysis, stupor, coma, muscle weakness and peripheral neuritis.<sup>2,3</sup> These manifestations are unusual in this disease entity, where the usual course is involvement of the regional lymph nodes about three weeks following a cat scratch or other mode of skin inoculation. Fever and generalized symptoms are common, but only rarely is the central nervous system involved.<sup>3</sup>

It is believed that this patient is the first reported in this country in whom the diagnosis of cat scratch encephalitis was made during the acute phase of the disease.

#### CASE REPORT

A 16 year old white male had been well until October 16, 1952, when he noted a hard, tender nodule in the right epitrochlear region. This nodule was about one inch in diameter. The only injury the patient recalled was a minor brush burn of the right elbow, acquired on the garage floor. This abrasion healed readily without evidence of infection. On October 20, enlargement of the glands in the right axilla was noted. On October 30 the patient consulted one of us (K. F. M.) because of the nodule. He had a fever of 102° F., which continued over 72 hours. He was treated with six doses of penicillin (400,000 units) intramuscularly. This was followed by oral terramycin, 250 mg. every six hours for 10 days. The nodule became smaller and firmer. There was subsiding tenderness in the right axilla until November 15; after that date there was more tenderness in the right axilla. The temperature fluctuated from 98.6° to 100° F. until November 20. The nodule remained tender, firm, warm and slightly reddened. On November 20 his temperature went to 104° F. and the nodule was incised. Because of the protracted course a culture was made of the greenish yellow purulent drainage from the abscess. This culture proved sterile. During this period the patient complained of general malaise but not of headache.

On November 23, at 8 a.m., the patient was found in a state of confusion. Within a very short time he was unable to respond to questions and was incapable of co-operation with his attendants. He was then referred to one of the authors (T. E. T., Jr.) and admitted to the Allegheny General Hospital, where he was found to have a normal temperature, a pulse rate of 120 and a respiratory rate of 28 per minute. He was vomiting and was incontinent of urine. He was very restless, had athetoid movements and moaned constantly until he was given 3½ gr. of sodium amytal intramuscularly about six hours following admission. The pupils were widely dilated and reacted weakly to light. The optic fundi were normal. The deep tendon reflexes were equal and active. The Oppenheim sign was positive bilaterally. The Babinski response was equivocal. Nuchal rigidity was not definite. Coma continued through the second hospital day, with definite nuchal rigidity. By the second hospital day the Babinski sign was present bilaterally and there was loss of deep tendon reflexes. The left eye deviated to the left for a few hours. After 48 hours consciousness returned. Nuchal rigidity disappeared. There was no deviation of the eyes. The left biceps reflex was slightly greater than the right. Both knee jerks were diminished. No Babinski sign was present. The patient swallowed water without dysphagia or nausea. He was able to answer simple questions and follow directions, but showed some dullness of intellect.

On the fifth day the pupils were round, equal and dilated, and reacted to light and accommodation. The biceps reflexes were equal and active. The abdominal reflexes were diminished on the left, especially on the lower left side. The knee jerks were equal but diminished. The Babinski was negative. The Achilles reflexes were equal and active. The extremities were normal except for a recently drained abscess in the right epitrochlear region. There was a mass of glands in the right axilla two and one-half inches in diameter, elevated one-half to three-fourths inches, tender

and nonfluctuating. There were no other enlarged lymph nodes in the cervical, left axillary, left epitrochlear or inguinal regions.

There were no abnormal findings in the nose, throat, ears, heart or lungs. The liver and spleen were not enlarged. There was no abdominal tenderness, mass or rigidity.

Following recovery from coma the patient showed gradual improvement in mental alertness and strength until his discharge from the hospital. Two instances of enuresis occurred during the hospitalization. Reflexes were normal on discharge and there was no muscle weakness. A neurologic examination six weeks later was normal. However, the patient's mother reported him to be irritable after returning home.

The history obtained from the mother stated that the boy had had a convulsive episode at the age of two years, when his fever was high due to furunculosis of the scalp. He had had chickenpox at the age of two and whooping cough at the age of five. A smallpox vaccination and diphtheria toxoid were administered at the age of six. He had had mumps and measles in his seventh year. In 1945 he had had an injection of tetanus antitoxin. There have been no subsequent immunization procedures, exanthemata or illnesses.

The patient had dressed two rabbits about 10 days before admission. However, this occurred about four weeks after the nodule in the right epitrochlear region appeared and at least three weeks after the enlarged right axillary nodes were found.

There have been cats in the household during all of the patient's life. During the preceding six months there was a mother cat and from two to eight kittens. The patient handled some of the cats daily. The mother cat died suddenly October 25, one month before the patient's admission and about nine days after the onset of the original abscess. The cat had not appeared to be ill prior to death, and poisoning was suspected. The patient had buried the dead animal but had not handled it, as it was placed in a box by another member of the family.

Spinal punctures were done on the first and the fourth hospital days. The results were as follows:

#### Spinal Fluid Examinations

	November 23, 1952	November 26, 1952
Pressure	50-125 mm.	95 mm.
Transparency	Clear	Clear
Cells	None	None
Pandy	Negative	Negative
Sugar	65 mg. %	—
Protein	42 mg. %	—
Chlorides	—	702 mg. %
Smear	No organism	No organism
Wassermann	Negative	
Lange gold	0000000000-0	
Culture	Negative	

A portion of the second specimen of fluid was sent to the Virus Research Laboratory of the University of Pittsburgh. A report by Ellen L. Moorhead for Dr. Jonas E. Salk states: "One-half of the total number of mice inoculated were either dead or sick enough to be sacrificed for examination three days after initial inoculation. A second passage of brain material from the sacrificed mice showed no sign of infection. It cannot be concluded that the original deaths resulted from the agent of cat scratch fever."

In the recent paper by Dr. Worth B. Daniels and Dr. Frank G. MacMurray<sup>3</sup> a personal communication from Dr. Robert Debré was cited which reported neurologic manifestations in this disease. Because of this report and history, cat scratch disease was considered a possible diagnosis.

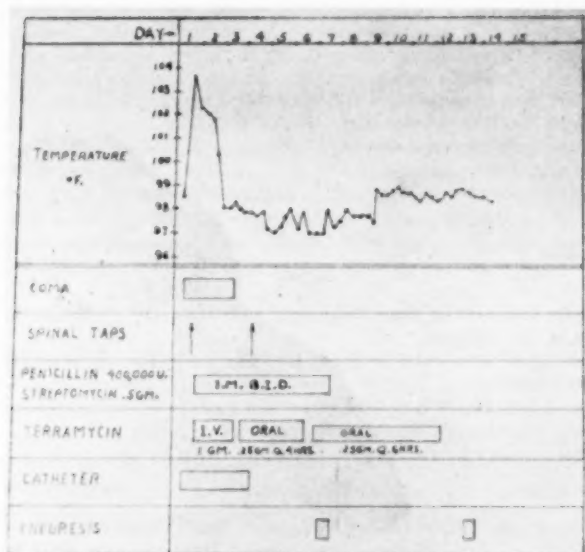


FIG. 1. Clinical course and antibiotic therapy.

Two cat scratch disease antigens were kindly furnished by Dr. Daniels and Dr. MacMurray for testing of the patient and controls. The first skin test with cat scratch antigen was done December 6, just before discharge from the hospital. The patient's mother was used as a control, although the dose given her was only 0.02 c.c. (since the antigen supply on hand was limited), while the patient was given the usual 0.10 c.c. At the end of 48 hours the patient showed a positive reaction, manifested by a central papule 5 mm. in diameter, surrounded by an area of erythema 1.5 cm. in diameter. The mother showed an indurated area 2 cm. in diameter but no papule. She had malaise and anorexia. For this reason a control test was done on another individual, using antigen from the same batch. There was no skin reaction.

One month later (January 8, 1953) the second proved antigen was used on the patient, his mother and another individual. The results were positive in the patient and his mother. The reaction in the patient consisted of a central papule 7 by 5 mm., and erythema 1 cm. in diameter. The reaction in the mother was a central papule 6 by 6 mm., and erythema 1.5 by 2 cm. The control was negative. Slight indurated papules still remained from the original skin tests done on the patient and his mother one month earlier.

The laboratory studies that follow were done either during or following hospitalization in an attempt to rule out other possible causes for the syndrome described.

#### Results of Serologic Tests

- Nov. 24 No agglutination with typhoid O or H, Paratyphoid A or B, *Brucella abortus* or *Bacilla proteus* O  $\times 19$ .
- Nov. 25 Negative agglutination *Pasteurella tularensis*.
- Dec. 4 Negative agglutination *Pasteurella tularensis*.
- Nov. 24 Heterophil antibody titer 1:16 dilution.
- Jan. 14 Heterophil antibody titer 1:16 dilution.

## Complement Fixation Tests

Dec. 22 Negative Lygranum.  
Jan. 23 Negative Lygranum.  
Jan. 19 Negative Eastern equine encephalomyelitis.  
Jan. 19 Negative Western equine encephalomyelitis.  
Jan. 19 Negative lymphocytic choriomeningitis.  
Jan. 19 Negative mumps.  
Jan. 23 Negative leptospirosis, microscopic agglutination negative.

## Frei Test

Dec. 10 Negative.

## X-Ray

Nov. 24 Bedside films of the skull failed to demonstrate any evidence of fracture of the bones of the cranium.

## Blood Counts

Nov. 23 W.B.C. 16,600.  
Nov. 23 R.B.C. 4,830,000, W.B.C. 11,550, Hb. 13.5 gm.  
Nov. 28 W.B.C. 12,350, neut. 58, eosin. 5, lymph. 31, mono. 6.  
Nov. 28 Sedimentation rate 30 mm./hr. V.P.C. 44 mm.

## Urinalyses

Nov. 23 Acid; sp. gr., 1.026; albumin, negative; sugar, negative; acetone, negative.  
Nov. 24 Acid; sp. gr., 1.033; albumin trace; sugar, trace; acetone, faint trace. Many R.B.C.'s, some W.B.C.'s; no casts.

## Blood Chemistry

Nov. 24 Nonprotein nitrogen, 39.7 mg. per cent; urea nitrogen, 25 mg. per cent; sugar, 103 mg. per cent.

## Blood Culture

Nov. 26 Blood culture drawn November 23, sterile.

An electroencephalogram (figure 2) was done on January 5, 1953, six weeks after the period of coma: "The findings were dominant 9/second moderate amplitude. Sporadic slow wave moderately high amplitude in left leads, frontal parietal and

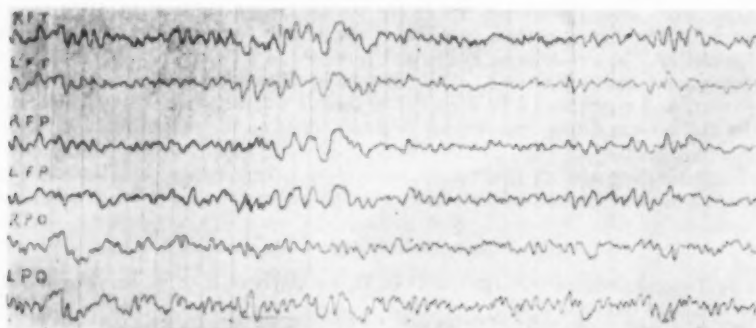


FIG. 2. Electroencephalogram taken six weeks following coma.

occipital. On hyperventilation slight increase of fast activity superimposed on dominant rhythm in parietal leads. After hyperventilation occasional runs of 4-5/second moderate amplitude in left fronto-temporal and left fronto-parietal areas. Impression: Abnormal record consistent with cerebral dysrhythmia but not consistent with convulsive state. There is no localization. Would suggest a repeat electroencephalogram in three months."

Treatment in the hospital consisted of early sedation, in the form of sodium amytal 3½ gr. intramuscularly as required for restlessness. Penicillin, 400,000 U, and streptomycin, 0.5 gm. intramuscularly, were administered every 12 hours for six days. Terramycin was given in two intravenous doses of 500 mg. 12 hours apart during coma, and was then continued orally in 250 mg. doses every four hours for three days, and then in the same dosage every six hours for six days.

#### COMMENT

The history of an abrasion followed by regional lymphadenitis with the development of sterile pus in an individual constantly exposed to cats is typical of cat scratch disease. The clinical picture is confirmed by two positive reactions to two separate specific antigens. The positive skin tests exhibited by the mother can be interpreted as due to an unnoticed benign form of the disease in the past. This is entirely possible, as she had had close contact with cats for 20 years. The individuals who gave negative control tests had had very slight contact with cats.

Though the patient had dressed rabbits during his illness, this occurred following the initial lesion. In addition, two negative agglutinations for tularemia rule out this disease. The negative results of the other tests above rule out the common forms of encephalitis and also infectious mononucleosis, lymphogranuloma venereum and the leptospiral diseases.

#### SUMMARY

We have reported the findings in a case of encephalitis in a boy with cat scratch disease. This is believed to be the first instance in this country in which the diagnosis of cat scratch encephalitis has been made during the acute phase of the disease. The syndrome should be considered in the differential diagnosis of coma and convulsive seizures. No conclusion has been drawn as to specific therapy, since several antibiotics were used in combination.

#### ACKNOWLEDGMENT

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3. Daniels, W. B., and MacMurray F. G.: Cat scratch disease; nonbacterial regional lymphadenitis: a report of 60 cases, *Ann. Int. Med.* **37**: 697, 1952.

## EDITORIAL

### IATROGENIC SALT DEPLETION

In the past several years we have developed important means of exploring and influencing our ionic equilibrium. Notable developments include the radioactive isotopes, the ion exchange resins (still much more useful in industry than in medicine), the vogue of salt restriction, the widespread use of potent diuretics and the clinical appreciation of hypokalemia and the low salt syndromes.

With the ever increasing employment of the principle of salt restriction or elimination in patients with congestive heart failure, hypertension, cirrhosis of the liver, nephrotic syndromes and other edematous states, it seems worth while to review the circumstances that favor and the dangers that surround salt depletion. No attempt has been made to cover the extensive literature on electrolyte balance and imbalance, nor will the mechanisms producing these disturbances be discussed—much of the material relevant to this phase is still highly theoretical. Attention will be focused on those depletion syndromes produced by the therapist and emphasis will be placed on the practical aspects of the problems involved.

The main therapeutic measures which may contribute to salt depletion are as follows:

- (1) stringent salt restriction;
- (2) energetic mercurial diuresis;
- (3) prolonged exchange resin therapy;
- (4) rehydration without proportionate restoration of salt, as in post-operative treatment with glucose in distilled water;
- (5) mechanical removal of large volumes of salt-containing fluids, as by paracentesis, Southey's tubes, or continuous gastric or intestinal suction without parallel administration of saline;
- (6) relief of severe urinary retention<sup>1</sup>;
- (7) ileostomy and other surgically produced fistulas;
- (8) broad spectrum antibiotic therapy complicated by diarrhea medicamentosa<sup>2</sup>;
- (9) sulfonamide therapy or transfusion complicated by lower nephron nephrosis.

It is obvious, but perhaps will bear emphasis, that depletion syndromes are most likely to occur when several of these factors coöperate, as when a cardiac patient is being treated with dietary sodium restriction, mercurial diuretics and exchange resins simultaneously; or when a cirrhotic is treated

<sup>1</sup> Holley, H. L.: The salt depletion syndrome, *Southern Med. J.* **45**: 153, 1952.

<sup>2</sup> Catanzaro, F. J., Ostfeld, A. M., and Bergner, G. E.: Occurrence of low salt syndrome during treatment with chloramphenicol, *J. A. M. A.* **149**: 571, 1952.

with these desalting measures as well as with repeated abdominal paracenteses. Or again the precipitating factor may be a phenomenon over which the physician has little or no control, as when vomiting (or simply not eating) complicates therapy with the resins, or when an August heat wave overtakes the energetically treated cardiac. In such situations the physician at least retains control over his prescription and he should moderate his anti-sodium measures until the additional threat has passed.

An important factor which often contributes to salt depletion is impaired renal efficiency, either functional or organic. Salt depletion can undoubtedly be produced, however, in the presence of normal kidney function.<sup>3</sup> It is also more likely to occur in elderly and arteriosclerotic individuals,<sup>4</sup> perhaps because their renal function has been undetectably compromised.

The untoward effects of desalting therapy have been recognized and emphasized for at least two decades. Popular recognition of salt depletion, however, dates from Schroeder's description in 1949 of the "low salt syndrome."<sup>5</sup> This syndrome is characterized chemically by a decrease in plasma sodium and chloride concentrations, acidosis, a decrease in urinary chlorides and an increase in blood urea; and clinically by weakness, drowsiness, muscular cramps, thirst unrelieved by water, anorexia, nausea and occasionally vomiting, decrease in urinary output and refractoriness to diuretics; a gain in weight and increasing edema sometimes occur<sup>6</sup>; restlessness, mental confusion, fall in blood pressure, increased pulse rate, and the full blown picture of shock and coma may supervene.

The treatment of this low salt syndrome is sometimes dramatically successful. Salt must be replenished, but water is not required. Salt is therefore administered while water is restricted. In mild cases this may be accomplished by giving salt by mouth, either in soups or in sugar-coated tablets.<sup>7</sup> In more severe cases salt must be given by vein and is then given in a 3 to 6 (usually 5) per cent solution. This solution should be slowly infused, not more than 200 c.c. being administered at a time. A total of 400 c.c. of the 5 per cent solution should be regarded as the maximum to be given in 24 hours. When success attends this therapy, there is rapid and striking clinical improvement and diuresis is initiated.

There are several methods for calculating the approximate salt deficit. As a rough guide it may be said that between 1 gm.<sup>8</sup> and 3 gm.<sup>8</sup> of salt will be needed to raise the sodium concentration by 1 mEq. per liter. Some

<sup>3</sup> McCance, R. A.: Experimental sodium chloride deficiency in man, *Proc. Roy. Soc., Lond., s.B.* **119**: 245, 1936.

<sup>4</sup> Jaffe, H. L., Master, A. M., and Dorrance, W.: The salt depletion syndrome following mercurial diuresis in elderly persons, *Am. J. M. Sc.* **220**: 60, 1950.

<sup>5</sup> Schroeder, H. A.: Renal failure associated with low extracellular sodium chloride. The low salt syndrome, *J. A. M. A.* **141**: 117, 1949.

<sup>6</sup> McLester, J. S., and Holley, H. L.: Salt depletion syndrome with increasing edema occurring during mercurial diuretic therapy, *Ann. Int. Med.* **36**: 562, 1952.

<sup>7</sup> Vogl, A.: *Diuretic therapy*, 1953, The Williams and Wilkins Co., Baltimore.

<sup>8</sup> Stock, R. J., Mudge, G. H., and Nurnberg, M. J.: Congestive heart failure. Variations in electrolyte metabolism with salt restriction and mercurial diuretics, *Circulation* **4**: 54, 1951.

workers<sup>9,10</sup> base their calculation on the weight of total body water (53 per cent of body weight):

A man weighing 60 kg. has about 32 kg. of total body water. If his serum sodium is 122 mEq./liter, then his total deficit of sodium is 142 minus  $122 = 20 \times 32 = 640$  mEq. One gram of NaCl contains 17.1 mEq. of sodium, and therefore 100 c.c. of 5 per cent salt solution contains  $17.1 \times 5 = 85.5$  mEq. This hypothetical patient will therefore require

$$640/85.5 \times 100 = \text{approx. } 750 \text{ c.c. of 5 per cent salt.}$$

Another method<sup>9,11</sup> is based on the weight of normal extracellular fluid (ECF); this equals approximately one fifth of "dry" body weight. The weight of accumulated edema is added to arrive at a total ECF weight. The serum deficit is then multiplied by this total ECF weight to obtain the total sodium deficit. To take a simple example:

A 60 kg. patient gains 10 kg. of edema fluid. His total ECF weight is then  $60/5 = 12 + 10 = 22$  kg. If his serum sodium is 122 mEq./liter he will require  $142 \text{ minus } 122 = 20 \times 22 = 440$  mEq. This patient will require, according to this method,

$$440/85.5 \times 100 = \text{approx. } 515 \text{ c.c. of 5 per cent salt.}$$

It is argued that the hypotonicity produced by sodium deficit is of the same magnitude in the intracellular as in the extracellular fluid, and that therefore the calculation of sodium deficit should be based on *total* body water. However this may be, it is found in practice that sometimes only a third or a half of the calculated dose is needed to restore sodium and chloride concentrations to normal.<sup>9</sup> It is therefore clear that the dose should be finally decided, not by any theoretical calculation, but by practical determinations of sodium and chloride levels. For this reason the calculated dose should be administered in divided amounts and punctuated by estimations of serum electrolytes.

It should be emphasized that hypertonic salt is not a sovereign remedy in all instances of salt depletion. Many authors comment on the disagreeable side-effects of this therapy, such as intolerable thirst and thrombophlebitis, and a number of cases treated energetically with 5 per cent salt have gone downward rapidly with increasing edema.<sup>12</sup>

It is important that the low salt syndrome be distinguished from hypochloremic alkalosis and from chronic dilution hyponatremia. *Hypochloremic*

<sup>9</sup> Citron, D., et al.: Congestive heart failure and hyponatremia: untoward effects of mercurial diuresis, *Ann. Int. Med.* **34**: 872, 1951.

<sup>10</sup> Welt, L. G.: Edema and hyponatremia, *Arch. Int. Med.* **69**: 931, 1952.

<sup>11</sup> Kattus, A. A.: Recent developments in the therapy of edema, *Med. Clin. North Am.* **36**: 953, 1952.

<sup>12</sup> Elkington, J. R., Squires, R. D., and Bluemle, L. W., Jr.: The distribution of body fluids in congestive heart failure. IV. Exchanges in patients, refractory to mercurial diuretics, treated with sodium and potassium, *Circulation* **5**: 58, 1952.

*alkalosis* is as common, if not commoner,<sup>7</sup> than the low salt syndrome. It has also been recognized for nearly three decades, but only recently has it attained popular understanding.<sup>13</sup> It is most often produced by mercurial diuresis, for the mercurials cause a proportionately greater elimination of chloride than of sodium.<sup>14</sup> The syndrome is not likely to attend diuretic therapy if (a) injections of the mercurial are spaced a few days apart permitting dietary replenishment of chloride; or (b) ammonium chloride is administered concurrently. This disturbance is characterized by a decreased serum chloride concentration while sodium remains at normal levels; alkalosis develops with increasing bicarbonate levels and urea retention; a concomitant decline in serum potassium often occurs. Schwartz<sup>13</sup> has helpfully tabulated the findings in typical cases of the low salt syndrome and hypochloremic alkalosis as follows:

Syndrome	Serum concentrations (mEq./l.)		
	Cl	HCO <sub>3</sub>	Na
Low salt syndrome	88	17	120
Hypochloremic alkalosis	88	37	140

The syndrome of hypochloremic alkalosis can usually be readily controlled. Milder cases may be given 3 to 6 gm. of ammonium chloride orally, in solution or in gelatine capsules—preferably not in the unpredictably absorbed enteric-coated tablets.<sup>7</sup> Patients who cannot tolerate ammonium chloride may be given dilute hydrochloric acid<sup>13</sup>: 20 c.c. of the 10 per cent acid (U.S.P.) is mixed in 600 to 1000 c.c. of water and given in divided amounts with meals. When the situation is urgent a 1 per cent solution of ammonium chloride in 5 per cent glucose may be given intravenously. This should be given slowly, at not more than 200 c.c. per hour and not exceeding a total of 1000 to 1500 c.c. in the day—the amount of ammonium ion released into the circulation by 10 to 15 gm. of ammonium chloride is apparently the maximum that the liver can detoxify (by conversion to urea) in 24 hours.<sup>7</sup>

*Chronic dilution hyponatremia* develops gradually and spontaneously in many patients with untreated heart failure<sup>7</sup> and in others receiving relatively conservative treatment. There is evidence that such a syndrome also develops in patients with chronic, debilitating illnesses associated with malnutrition and wasting. The mechanisms involved in the production of this chemical syndrome are discussed in detail by Welt.<sup>10</sup> In whatever circumstances it develops, chronic dilution hyponatremia indicates a grave prognosis although symptoms from the hyponatremia per se are less likely to appear than in the acute depletion syndrome. The presence of such symptoms as somnolence, clouding of consciousness, coma, falling blood pressure and nitrogen retention, all suggest an acute rather than a chronic hyponatremia.

<sup>13</sup> Schwartz, W. B.: The role of electrolyte balance in the response to mercurial diuretics in congestive heart failure, *Bull. New Eng. Med. Cent.* 12: 213, 1950.

<sup>14</sup> Schwartz, W. B., and Wallace, W. M.: Electrolyte equilibrium during mercurial diuresis, *J. Clin. Investigation* 30: 1089, 1951.

In the chronic hyponatremia of heart failure, hypertonic saline is apparently not the treatment of choice. On the other hand full digitalization at this stage may restore cardiac compensation with loss of edema and a return of serum sodium concentration to normal levels. Awareness of this syndrome makes it obvious that it is wisest to examine the electrolyte pattern in any patient in failure before instituting a regimen of drastic salt restriction plus frequent mercurial diuretics.<sup>7</sup>

Hyponatremia can be diagnosed with certainty only by a direct estimation of the serum sodium. Indirect calculation from the sum of bicarbonate and chloride concentrations<sup>15</sup> should not be regarded as an adequate substitute for direct sodium estimation. Indirect estimation from the concentration of chlorides alone may be even more dangerously misleading, for the chlorides may fall both in metabolic alkalosis and in respiratory acidosis while sodium concentrations remain normal.

While the syndromes attending the overenthusiastic use of diuretics and salt restriction are complex enough, the addition of exchange resins to the salt-depleting regimen may produce even more profound and widespread electrolytic changes—hyperchloremic acidosis, hypokalemia and hypocalcemia may complicate the picture.<sup>16, 17, 18</sup> To date these chemical changes have most often been recognized without severe accompanying symptoms.

*Hyperchloremic acidosis* is a logical result of the predominant removal of cation by the resin exchangers and is obviously most likely to occur in patients with impaired renal function. Intermittent use of the resins, with concurrent mercurial diuresis to eliminate a greater burden of chloride, will help to avoid this complication of resin therapy. Hyperchloremic acidosis has also recently been described as an important complication of ureterosigmoidostomy, as a result of undue absorption of urinary chlorides by the colon.<sup>19</sup>

*Hypokalemia* results from absorption of potassium by the resins and is only partly offset by the use of potassium-containing exchangers. It is important that an adequate dietary intake of potassium should supplement the use of even this type of resin. An excellent reason for taking pains to avoid potassium depletion in congestive heart failure is that digitalis intoxication is more easily produced in the absence of adequate potassium con-

<sup>15</sup> Hald, P. M., Heinsen, A. J., and Peters, J. P.: The estimation of serum sodium from bicarbonate plus chloride, *J. Clin. Investigation* **26**: 983, 1947.

<sup>16</sup> Gill, R. J., and Duncan, G. G.: Arterial hypertension—the therapeutic effect of cation-exchange resins, *New Eng. J. Med.* **247**: 271, 1952.

<sup>17</sup> Greenman, L., Shaler, J. B., and Danowski, T. S.: Biochemical disturbances and clinical symptoms during prolonged exchange resin therapy in congestive heart failure, *Am. J. Med.* **14**: 391, 1953.

<sup>18</sup> Weston, R. E., et al.: Metabolic studies on the effects of ion exchange resins in edematous patients with cardiac and renal disease, *Am. J. Med.* **14**: 404, 1953.

<sup>19</sup> Editorial: Hyperchloremic acidosis following ureterosigmoidostomy, *J. A. M. A.* **152**: 334, 1953.

centrations. As a corollary of this, digitalization can be pushed further with less danger of toxicity when potassium levels are normal.<sup>20, 21</sup>

Clinically, hypokalemia is characterized by weakness, malaise, rapid pulse, shallow respiration, stupor, the so-called "fish-mouth" expression and muscular paralysis. Electrocardiographic changes may be diagnostically helpful. When hypokalemia has been diagnosed, potassium chloride is the drug of choice if the deficiency is part of a hypochloremic alkalosis, while potassium citrate or acetate is preferred in acidotic cases. The usual daily dose is 3 to 6 grams orally, but this must be regulated by frequent determinations of serum potassium levels.<sup>7</sup>

The development of *hypocalcemia* is most likely to attend the use of sulfonic forms of the cationic exchangers, but it may also occur with prolonged use of the carboxylic resins.<sup>17</sup> The clinical development of tetany is unusual, and it is worth noting in passing that two of the often associated electrolyte disturbances, hypokalemia and acidosis, militate against the development of clinical tetany. It is believed that the problem of hypocalcemia is likely to become more troublesome as time goes on and more patients are maintained on resins for prolonged periods. Nor is the solution simply to give additional calcium by mouth, for if this cation is present in the intestinal canal in excess, it will presumably compete with sodium for the exchanger and thus defeat the primary purpose of resin therapy.<sup>17</sup>

As it has been demonstrated that not only sodium and chloride, but also potassium and calcium are excreted in increased amounts in mercurial diuresis,<sup>22</sup> it is obvious that hypokalemia and hypocalcemia are more likely to make their appearance when mercurials are used together with resins.

As the anti-sodium campaign increases in tempo and widens its scope, we must be watchful for signs and symptoms of salt depletion. Low sodium foods are becoming more available; ingenious low sodium diets are being devised; the mercurials are enjoying increasing popularity and the exchange resins have entered the lists. Meanwhile paracenteses, suction, fistulas, vomiting, diarrhea and heat waves all continue to exert their desalting influences on our patients' internal environments. There is therefore certain to be an increasing number of induced salt depletion syndromes, and every clinician should be well versed in their recognition and treatment, but most of all in their prevention.

H. J. L. M.

<sup>20</sup> Weston, R. E., et al.: Mechanisms contributing to unresponsiveness to mercurial diuretics in congestive failure, *J. Clin. Investigation* 31: 901, 1952.

<sup>21</sup> Lown, B., et al.: Interrelation between potassium and digitalis toxicity in heart failure, *Proc. Soc. Exper. Biol. and Med.* 76: 797, 1951.

<sup>22</sup> Blumgart, H. L., et al.: Action of diuretic drugs. I. Action of diuretics in normal persons, *Arch. Int. Med.* 54: 40, 1934.

## REVIEWS

*Second Annual Report on Stress.* By HANS SELYE, M.D., Ph.D. (Prague), D.Sc. (McGill), F.R.S. (Canada), and ALEXANDER HORAVA, M.D. (Lausanne). 526 pages; 17.5 x 25.5 cm. Acta, Inc., Montreal. 1952. Price, \$10.00, plus 34 cents mailing charges.

Anyone who wants a reliable and all inclusive guide to the recent literature on stress will find this book invaluable, regardless of whether his interests center on the clinic or the laboratory. The specialist certainly cannot do without it. As the Second Annual Report on Stress, it supplements the two previous volumes of this series.

The textual material is limited and makes up only 10 per cent of the total length of the book. The rest is devoted mainly to a section entitled, "Special Physiology and Pathology of Stress." Here are references to all of the literature which appeared in this field during the last year or so, arranged in such way as to show how the various organs, organ systems, bodily responses, bodily constituents and bodily mechanisms are affected by any sort of stress. For instance, if one should wish to know how exposure to cold affects the mammalian heart, it is only necessary to look under the part assigned to the heart in the section on the cardiovascular system, run his eye down the column until it meets the heading marked "Cold," and then check the references. Thus the entire literature is indexed and cross-indexed until it is difficult to see how any interrelationship, however minute, can escape detection. It is an amazing job of cataloging.

Each section also contains references to pages in the preceding volume so that the investigator can select with a minimum of effort all the papers pertinent to the subject in hand which have appeared anywhere. In addition there is a bibliography supplementing previous bibliographies and containing a complete list of all papers published since the appearance of the last volume. For the most part the papers in the present volume came out in 1951 or 1952, but there is a scattering which appeared either earlier or later.

There is also a carefully constructed index of the more or less conventional sort. Dr. Selye and his associates deserve only the highest praise for their monumental efforts in making the world's literature on stress readily available to their colleagues.

As already mentioned, the textual material is slight and is devoted largely to an explanation of the book, how to use it, and an apology for writing it. There is also a summary of the General Adaptation Syndrome as it stands at the moment of writing and a resumé of the principal objections to it. The book concludes with a section entitled "After Thoughts," which contains a sketch for a unified theory of medicine which will no doubt provoke further discussion in this controversial field. The format, typography and binding are similar to the companion volumes in the series.

DIETRICH C. SMITH

*Brain and Behaviour: Induction as a Fundamental Mechanism of Neuro-Psychic Activity; An Experimental and Clinical Study with Consideration of Educational, Mental-Hygienic and General Sociological Considerations.* By N. E. ISCHLONDSKY, M.D. 184 pages; 15.5 x 25.5 cm. C. V. Mosby Co., St. Louis. 1949. Price, \$7.50.

This book consists of three essays: (1) Brain Mechanism of Coronary Disease, and two appendices; (2) From the Conditioned Reflex to the Science of Brain Dynamics; (3) Reflexologic Bases of Personality. The main section (pages 1-87) relates coronary disease to a violation of conditional reflex principles; analyzes the

rapid increase of coronary disease; recommends therapy based on the described principles. For his principles Ischlonsky takes the ones on which Pavlov placed the chief emphasis, viz., irradiation of excitation and inhibition and induction (which to Ischlonsky is the most important). This can be illustrated as follows: excitation may spread in the brain to either the vagal or the sympathetic centers with the corresponding effect on heart rate and compensatorily on blood pressure. If induction is in the ascendancy, however, positive excitation would cause not excitation of the vagus but the opposite process, viz., inhibition with a consequent rise in heart rate. Ischlonsky continues with a discussion of other principles described by Pavlov in the evolution of the experimental neurosis—collision of excitation and inhibition in time and space.

The applications to American life are more interesting than scientifically validated. Thus, the irritation which Ischlonsky observes especially in Americans when they are interrupted or asked to change their accustomed routine ("rhythm") is referred to as a want of "inhibitory training." For the sake of the heart "it really pays to be patient, courteous and tactful." Later in the book, where alcohol and especially tobacco are incriminated as etiologic factors of coronary disease, the essential harm of tobacco is the "social discourtesy . . . and destructive effect it exerts upon the nervous balance." "When, for instance, people light their cigarettes, cigars or pipes, in a crowded elevator where the total volume of air is not more than a few cubic feet, and the burning cigarettes, in addition, are pressed against the overcoats of other people, it is obviously a condition which can hardly be qualified as civil." (Ischlonsky might have added that this incivility is perhaps even more conducive to nervous imbalance and coronary disease of the unwilling but long-suffering non-smoker with his alertness for detecting the smoker's multifarious variations for inflicting social discourtesies!)

In the chapter on the Statistical Data relating to coronary heart disease, we are confronted with some startling facts. Heart disease (all forms) in the U.S. has moved from third place in 1900 (8 per cent) to first place in 1930 (19 per cent) and is steadily increasing (33 per cent in 1948). Some interesting data emerge in the analysis by age, sex, race. Whereas coronary disease was practically unknown except in advanced age (unless due to syphilis), it has now invaded the younger ages to an alarming degree. In the U.S.A. it is far less common in Chinese, Negroes, and Indians (in the order given) than in the whites. It is two and one-half times more frequent in American males than females because the "American woman has a more rhythmic collision (in the sense of balanced excitation and inhibition) than the contemporary American man . . . and the woman has a more rhythmic life than the contemporary American man. Of no less importance is the fact that the woman, due to her upbringing, possesses a much better trained inhibitory mechanism for the suppression of all those little irritations in everyday life which the man has never learned to combat." It is said that Negroes in Africa do not show coronary disease in the younger groups "owing to the protective effect of a strong natural *rhythmicity* inherent in the nervous organization of the Negro people."

Owing to the stress of the wars in England the mortality due to coronary disease has mounted from 29 per million in 1921 to 148 in 1930 to 996 in 1949 in spite of the traditionally "well trained inhibitory process" of the Englishman. In the "ideal" country of Switzerland, "where for centuries she has lived her own life" and where the people "display a high rhythmical development of nervous activity and a frictionless cooperation of the excitatory and inhibitory processes," coronary mortality is only one-half as much as it is in England and one quarter as much as in the U.S.A. (1945 data).

The chapter on therapy not only draws the obvious conclusion from the theoretical and factual principles evolved earlier, but it adds a note about the use of bromides

for the excitatory and caffeine for the inhibitory types. Pavlov had previously emphasized the regulation of the dosage of bromides for inhibitory types—Ishlonsky goes further and says that the ratio of dose may have to be as great as 20:1 in different constitutional types.

The two appendices will be of less interest to the internist than is the section on heart disease, as they are concerned chiefly with the theoretical discussion of Pavlovian conditional reflex principles. However, the psychiatrist and the psychologist will find much here to ponder over.

This book is concisely written and easy to read. The style is clear and animated. It raises many exciting problems about the relation of coronary disease to stress. It is, to this reviewer, provocative rather than definitive.

W. HORSLEY GANTT

*Elementary Statistics with Applications in Medicine.* By FREDERICK E. CROXTON, Ph.D., Professor of Statistics, Columbia University. 376 pages; 22 × 14.5 cm. Prentice-Hall, Inc., New York. 1953. Price, \$10.00.

As the title warns, the material discussed in the above book is "elementary statistics with applications in medicine" and *not* medical statistics. The text is essentially a condensation of an earlier book by the same author (with Cowden), entitled *Applied General Statistics*, which deals with economic and business statistics. The principal changes are a fuller discussion of statistical tests for proportions, the use of examples with a medical flavor, and omission of much of the material in the earlier book. Such superficial changes are not enough to adapt the material to the needs of doctors and medical students.

The problems in the statistical interpretation of medical studies are somewhat different from the corresponding problems in fields such as economic statistics. The two principal sources of difficulty in medical data are biased sampling and inadequate controls. The nature of these difficulties is not discussed and, in fact, an "historical control" is used in an example (page 267).

The book has its virtues as a treatment of general elementary statistics, especially in dealing with such topics as tables and graphs, etc., but the discussion is nowhere near as complete as the corresponding treatment in *Applied General Statistics*, which is three times as long and costs two dollars less.

I. B.

*Roentgen, Radium and Radioisotope Therapy.* By A. J. DELARIO, M.D., Member of American College of Radiology; Radiological Society of North America; Head of Therapeutic Radiology, St. Joseph Hospital, Paterson, N. J. 371 pages; 15.5 × 24.5 cm. Lea & Febiger, Philadelphia. 1953. Price, \$7.50.

This book approaches irradiation therapy from a slightly different viewpoint than others on this subject. Emphasis throughout is on the fundamental physical principles of irradiation. These are completely covered from the standpoint of a radiotherapist rather than a physicist. Although it contains no specific information which could not be obtained elsewhere, the material is presented in a more practical, clear and concise manner than in other sources.

While the author has superbly discussed the basic and physical principles of irradiation therapy, he has almost completely ignored the clinical aspects. In one chapter the radiosensitivity of various lesions is discussed rather superficially in groups, with the total dosage needed in each group. Total dosages are mentioned in a few other chapters, but the clinical technics and responses are inadequately discussed. In most instances the planning of therapy is not mentioned.

This text is well illustrated for comparison of the physical and biological aspects of all types of radiation. Radiologists and other physicians interested in irradiation

therapy will find this a useful reference in regard to physical principles but will find it inadequate from a clinical standpoint.

J. M. D.

*A Manual of Clinical Allergy.* By JOHN M. SHELDON, M.D., ROBERT G. LOVELL, M.D., and KENNETH P. MATHEWS, M.D. 413 pages; 16.5 × 25.5 cm. W. B. Saunders Co., Philadelphia. 1953. Price, \$8.50.

This new handbook on the practice of allergy is a distinctly valuable addition to the library. It is a well written and well produced book, with a somewhat different emphasis from that of other allergic texts.

If this book has a single outstanding characteristic, it is that it is essentially practical. In keeping with this, particular emphasis is placed on such subjects as pollen and mold identification, the preparation of testing and treatment extracts and the inventory of necessary equipment for an allergist's office. Pulmonary function tests are discussed at unusual length and the subject of allergy to plastics is given detailed consideration. Recently growing developments in the field of allergy, such as endocrine factors in hypersensitivity, the collagen diseases, vascular allergy and drug allergy, receive more space than in most standard texts.

On the other hand, in maintaining their standard of practical briefness, the authors do not enter into lengthy discussions of immunologic theory and other controversial matters. Perhaps the best way to illustrate the authors' preoccupation with practical procedures is to draw attention to the fact that, while the clinical aspects of hay fever, allergic rhinitis and bronchial asthma together are dealt with in but 10 pages, no less than 35 are devoted to the technics of patch testing.

Among the excellent material here presented is a highly practical and rational discussion of the much abused antihistamine drugs and an admirable section on the identification of pollens, graced by superb photographs which will be of great value at the pollen-counter's elbow.

Throughout the work the reader enjoys the impression that the subject is being competently and, within the authors' designed framework, thoroughly handled. The book is intended primarily for the physician interested in establishing an allergy practice, or in devoting at least part of his time to the treatment of allergic patients. Certainly to such physicians this lucid and practical presentation of allergic matters should be of great value.

H. J. L. M.

*Textbook of Virology for Students and Practitioners of Medicine.* 2nd Ed. By A. J. RHODES, M.D., F.R.C.P. (Edin.), Research Associate, Connaught Medical Research Laboratories and Professor of Virus Infections, School of Hygiene, University of Toronto, and C. E. VAN ROOYEN, M.D., D.Sc., (Edin.), M.R.C.P. (Lond.), Research Member, Connaught Medical Research Laboratories and Professor of Virus Infections, School of Hygiene, University of Toronto. 561 pages; 15.5 × 23.5 cm. Williams and Wilkins Company, Baltimore. 1953. Price, \$8.00.

This excellent text presents a modern, concise account of the essential features of virus and rickettsial infections of man. As stated in the preface, this book is written primarily for the medical student and practitioner of medicine. The authors have a larger and more complete work entitled *Virus Diseases of Man* available for those interested in more extensive reading in the field.

The present volume is superior in many ways to the first edition which appeared in 1949. The authors have given more emphasis to the virus and rickettsial diseases occurring in North America and to the importance of laboratory diagnosis in these

diseases. A most welcome addition is the selected bibliographies for further reading which have been appended to each chapter.

The revised chapter on influenza is made more complete by the inclusion of data from many recent pertinent publications. Among these are some of the studies of Sir MacFarlane Burnet concerning influenza virus variants and a clearer concept of the present knowledge of virus immunity. The discussions of poliomyelitis, yellow fever and pneumonitis of viral origin have been expanded to include material which has appeared in recent medical literature. An important addition is an evaluation of broad spectrum antibiotics as they apply to the therapy of virus and rickettsial diseases.

The text includes new chapters devoted to Rickettsialpox, the Coxsackie viruses and encephalomyocarditis-myelitis of animals, as well as a discussion of the laboratory diagnosis of virus diseases. The latter subject is an essential component of any modern textbook of virology.

The subject material is well presented, readable and divided into 12 sections of several chapters each. Numerous illustrations enhance the understanding of what might otherwise be a difficult subject.

The book is timely, complete in coverage within its stated scope, moderately priced and fills a great need not only for a better understanding of virus and rickettsial diseases by the medical student but by the instructor and practitioner of medicine as well.

J. B. W.

*Dermatology: Essentials of Diagnosis and Treatment.* By MARION B. SULZBERGER, M.D., and JACK WOLF, M.D. 592 pages; 15.5 × 23.5 cm. The Year Book Publishers, Inc., Chicago. 1952. Price, \$10.00.

This is the fourth edition of this book which first appeared in 1940. The present edition brings the text up to date in methods of diagnosis and adds the latest therapeutic agents including cortisone and ACTH. The book is designed for the medical student and general practitioner, being written in a simple straightforward style. The graduate, student or resident in dermatology will find it valuable also.

The chapters on Principles of Diagnosis, Principles of Topical Medications and Principles of other measures, such as various types of radiation therapy, are written clearly and are well illustrated. Diseases are divided into twelve groups, each group forming a chapter. Each chapter relates the diagnostic criteria for the group of diseases and the methods of therapy for them and allied diseases which have some common similarity. All possible new approaches to therapy are included, even selenium sulfide in seborrheic dermatitis. This book is a concise approach to modern dermatology and on the desk of most practitioners will serve as a handy source of reference.

E. S. B.

#### BOOKS RECEIVED

Books received during May are acknowledged in the following section. As far as practicable those of special interest will be selected for review later, but it is not possible to discuss all of them.

*An Atlas of the Commoner Skin Diseases, with 147 Plates Reproduced by Direct Colour Photography from the Living Subject.* 4th Ed. By HENRY C. G. SEMON, M.A., D.M. Oxon., F.R.C.P., London, Consulting Physician for Diseases of the Skin, etc.; Colour Photography originally directed by the late ARNOLD MORITZ, B.A., M.B., B.C. Cantab. 371 pages; 25.5 × 18.5 cm. 1953. The Williams & Wilkins Company, Baltimore. Price, \$13.50.

*Blood and Blood Derivatives Program (Revised Edition—1953). Federal Civil Defense Administration (Technical Manual) TM-11-5.* 203 pages; 23.5 × 15 cm. (paper-bound). 1953. United States Government Printing Office, Washington, D. C. For sale by the Superintendent of Documents, U. S. Government Printing Office, Washington-25, D. C. Price, 40 cents.

*Chronic Pulmonary Emphysema: Physiopathology and Treatment. Modern Medical Monographs 8.* By MAURICE S. SEGAL, M.D., Clinical Professor of Medicine, Tufts College Medical School, etc.; and M. J. DULFANO, M.D., Resident, Department of Inhalational Therapy, Boston City Hospital, etc. 180 pages; 22.5 × 14.5 cm. 1953. Grune & Stratton, Inc., New York. Price, \$5.50.

*Clinical Cardiology.* Edited by FRANKLIN C. MASSEY, A.B., M.D., Assistant Professor of Medicine, Hahnemann Medical College, Philadelphia, Pennsylvania. 1,100 pages; 23.5 × 15.5 cm. 1953. The Williams & Wilkins Company, Baltimore. Price, \$13.50.

*Dermatology in General Practice.* By JACOB HYAMS SWARTZ, M.D., Assistant Professor of Dermatology, Harvard Medical School and Post-graduate School, etc.; Foreword by C. GUY LANE, M.D., Professor Emeritus, Department of Dermatology, Harvard Medical School, etc. 581 pages; 23.5 × 15.5 cm. 1953. The Williams & Wilkins Company, Baltimore. Price, \$11.00.

*Differentialdiagnose innerer Krankheiten: Eine Kurzgefasste Darstellung für Ärzte und Studierende.* By DR. ROBERT HEGGLIN. 556 pages; 24.5 × 17.5 cm. 1953. Georg Thieme Verlag, Stuttgart; Agents for U. S. A.: Grune & Stratton, Inc., New York. Price, Ganzleinen DM 55.—

*Diseases of Muscle: A Study in Pathology.* By RAYMOND D. ADAMS, M.A., M.D., Associate Clinical Professor of Neurology, Harvard Medical School, etc.; D. DENNY-BROWN, M.D., D.Phil., F.R.C.P., James Jackson Putnam, Professor of Neurology, Harvard Medical School, etc.; and CARL M. PEARSON, M.D., Former Resident in Pathology, Mallory Institute of Pathology, Boston City Hospital. 556 pages; 24 × 16 cm. 1953. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York. Price, \$16.00.

*Diuretic Therapy: The Pharmacology of Diuretic Agents and the Clinical Management of the Edematous Patient.* By ALFRED VOGL, M.D., Assistant Professor of Clinical Medicine, New York University College of Medicine, etc. 248 pages; 23.5 × 15.5 cm. 1953. The Williams & Wilkins Company, Baltimore. Price, \$5.00.

*The Epidemiology of Health. A New York Academy of Medicine Book.* IAGO GALDSTON, M.D., Editor. 197 pages; 22.5 × 14 cm. 1953. Health Education Council, New York. Price, \$4.00.

*Gout and Gouty Arthritis. Modern Medical Monographs 7.* By JOHN H. TALBOTT, M.D., Professor of Medicine, The University of Buffalo School of Medicine, etc. 92 pages; 22.5 × 14 cm. 1953. Grune & Stratton, New York. Price, \$4.00.

*Handbook of Treatment of Acute Poisoning.* By E. H. BENSLEY, M.B.E., B.A., M.D., F.A.C.P., Director, Department of Metabolism and Toxicology, The Montreal General Hospital, etc.; and G. E. JORON, B.A., M.D., C.M., Dip. Int. Med., Junior Assistant, Department of Medicine and Department of Metabolism and Toxicology, The Montreal General Hospital, etc. 201 pages; 17.5 × 11.5 cm. 1953. Renouf Publishing Company, Ltd., Montreal. Price, \$2.50.

- Human Factors in Air Transportation: Occupational Health and Safety.* By ROSS A. MCFARLAND, Ph.D., Associate Professor of Industrial Hygiene, Harvard School of Public Health. 830 pages; 25.5 x 18.5 cm. 1953. McGraw-Hill Book Company, Inc., New York. Price, \$13.00.
- The Incidence of Peptic Ulcer in Denmark: A Statistical Study on the Clinical Incidence of Gastric and Duodenal Ulcer in the Danish Population in 1940 and 1948.* By GUNNAR ALSTED, M.D., Privat-Docent at the University of Copenhagen, etc.; with Prefaces by DR. JOHNS. FRANDSEN and PROFESSOR E. MEULENGRACHT. 88 pages; 25 x 17 cm. (paper-bound). 1953. Danish Science Press, Ltd., Copenhagen. Price, \$2.25.
- Influenza and Other Virus Infections of the Respiratory Tract.* By C. H. STUART-HARRIS, M.D., F.R.C.P., Professor of Medicine, University of Sheffield; with a Foreword by C. H. ANDREWES, M.D., F.R.C.P., F.R.S., Deputy Director, National Institute for Medical Research. 235 pages; 22.5 x 14 cm. 1953. The Williams & Wilkins Company, Baltimore. Price, \$6.00.
- Lectures on the Scientific Basis of Medicine. Volume I, 1951-52. British Postgraduate Medical Federation, University of London.* 403 pages; 22 x 14.5 cm. 1953. The Athlone Press, University of London; available in U. S. A. from John de Graff, Inc., New York. Price, \$6.00.
- The Low Sodium Cook Book: How to Prepare Tasteful Meals for the Low Sodium or Low Salt Diet—Including Suggestions for the Low Sodium, Low Fat, Low Cholesterol Diet.* By ALMA SMITH PAYNE, M.A., and DOROTHY CALLAHAN, B.S., Research Dietitian, Massachusetts General Hospital; with an Introduction by FRANCIS L. CHAMBERLAIN, M.D., M.Sc.D., University of California Medical School. 477 pages; 20.5 x 13.5 cm. 1953. Little, Brown & Company. Price, \$4.00.
- Nervous System. Volume I, The Ciba Collection of Medical Illustrations.* A Compilation of Pathological and Anatomical Paintings Prepared by FRANK H. NETTER, M.D.; with a Foreword by JOHN F. FULTON, M.D., Sterling Professor of the History of Medicine, Yale University School of Medicine. 143 pages; 31.5 x 24.5 cm. 1953. Commissioned and published by Ciba Pharmaceutical Products, Inc., Summit, New Jersey. Price, \$6.00.
- Die Neuzeitlichen Brustwand- und Extremitäten-Ableitungen in der Praxis.* By PROF. DR. HERBERT REINDELL and DR. HELMUTH KLEPZIG; with an Introduction by PROF. DR. LUDWIG HEILMEYER. 188 pages; 25 x 17.5 cm. 1953. Georg Thieme Verlag, Stuttgart; agents for U. S. A.: Grune & Stratton, Inc., New York. Price, Ganzleinen DM 24.60.
- The Physician in Atomic Defense: Atomic Principles, Biologic Reaction and Organization for Medical Defense.* By THAD P. SEARS, M.D., F.A.C.P., Associate Clinical Professor of Medicine, University of Colorado School of Medicine, etc.; with a Foreword by JAMES J. WARING, M.D., M.A.C.P., Professor of Medicine, University of Colorado School of Medicine. 308 pages; 21 x 14 cm. 1953. The Year Book Publishers, Inc., Chicago. Price, \$6.00.
- Potassium Metabolism: Report of the Sixth M & R Pediatric Research Conference.* 46 pages; 23 x 15 cm. (paper-bound). 1953. M & R Laboratories, Columbus, Ohio. Available to physicians on request, without cost.
- Psychiatric Dictionary, with Encyclopedic Treatment of Modern Terms.* 2nd Ed., with Supplement. By LELAND E. HINSIE, M.D., Formerly Professor of Psy-

- chiatry, College of Physicians and Surgeons, Columbia University, New York, etc.; and JACOB SHATZKY, Ph.D., Research Librarian, New York State Psychiatric Institute and Hospital. 781 pages; 24.5 x 16 cm. 1953. Oxford University Press, New York. Price, \$15.00.
- Segundo Congreso Uruguayo de Cirugía, 5 al 8 de Diciembre, 1951.* 639 pages; 24 x 16.5 cm. (paper-bound). 1953. Secretaria General, Montevideo.
- The Suprarenal Cortex: Proceedings of the Fifth Symposium of the Colston Research Society, held in the University of Bristol, April 1st-4th, 1952.* Edited by J. M. YOFFEY. 232 pages; 25.5 x 19 cm. 1953. Academic Press, Inc., New York. Price, \$6.80.
- Transactions of the American College of Cardiology. Vol. II—1952.* Editor: BRUNO KISCH, M.D. 252 pages; 25 x 16.5 cm. (paper-bound). 1953. Published by American College of Cardiology, New York. Price, \$5.00.
- Tumors of the Central Nervous System (Atlas of Tumor Pathology, Section X, Fascicles 35 and 37).* By JAMES W. KERNOHAN, M.D., Section on Pathologic Anatomy, Mayo Clinic, Rochester, Minnesota, etc.; and GEORGE P. SAYRE, M.D., Section on Pathologic Anatomy, Mayo Clinic, Rochester, Minnesota, etc. 129 pages; 26 x 20 cm. (paper-bound). 1952. Published by the Armed Forces Institute of Pathology under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C. Price, 90 cents.
- Tumors of the Lower Respiratory Tract (Atlas of Tumor Pathology, Section V, Fascicle 17).* By AVERILL A. LIEBOW, M.D., Professor of Pathology, Yale University School of Medicine. 189 pages; 26 x 20 cm. (paper-bound). 1952. Published by the Armed Forces Institute of Pathology under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C. Price, \$1.25.
- Tumors of the Male Sex Organs (Atlas of Tumor Pathology, Section VIII, Fascicles 31b and 32).* By FRANK J. DIXON, M.D., Professor of Pathology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; and ROBERT A. MOORE, M.D., Professor of Pathology, Washington University School of Medicine, St. Louis, Missouri. 179 pages; 26 x 20 cm. (paper-bound). 1952. Published by the Armed Forces Institute of Pathology under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C. Price, \$1.50.
- Tumors of the Parathyroid Glands (Atlas of Tumor Pathology, Section IV, Fascicle 15).* By BENJAMIN CASTLEMAN, M.D., Acting Chief, Department of Pathology and Bacteriology, Massachusetts General Hospital, etc. 74 pages; 26 x 20 cm. (paper-bound). 1952. Published by the Armed Forces Institute of Pathology under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C. Price, 65 cents.
- Tumors of the Thyroid Gland (Atlas of Tumor Pathology, Section IV, Fascicle 14).* By SHIELDS WARREN, M.D., Professor of Pathology, Harvard Medical School, etc.; and WILLIAM A. MEISSNER, M.D., Assistant Professor of Pathology, New England Deaconess Hospital, Boston, Massachusetts. 97 pages; 26 x 20 cm. (paper-bound). 1953. Published by the Armed Forces Institute of Pathology under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C. Price, \$1.75.

## COLLEGE NEWS NOTES

### NEW LIFE MEMBERS

The College is pleased to announce that the following Fellows have become Life Members of the American College of Physicians since the publication of the list in last month's issue of this journal:

Dr. Marion B. Sulzberger, New York, N. Y.  
Dr. Arthur Merrimon Freeman, Jr., Birmingham, Ala.  
Dr. George Hollander, Philadelphia, Pa.  
Dr. Lindon L. Davis, Levittown, N. Y.

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### COMING ACP REGIONAL MEETINGS, 1953

WEST VIRGINIA, White Sulphur Springs, July 24; Paul H. Revercomb, M.D., Governor  
NORTH DAKOTA, Fargo, Sept. 12: Robert B. Radl, M.D., Governor  
ARKANSAS-OKLAHOMA, Tulsa, Sept. 19: A. A. Blair, M.D., and Wann Langston, M.D., Governors  
OHIO, Dayton, Oct. 9; Charles A. Doan, M.D., Governor; A. B. Brower, M.D., Chairman  
WESTERN NEW YORK, Syracuse, Oct. 9; Edward C. Reifenshtein, M.D., Governor  
MONTANA-WYOMING, Missoula, Oct. 9-10; Harold W. Gregg, M.D., Governor  
PUERTO RICO, San Juan, Oct. 15, 16, 17; R. Rodriguez-Molina, M.D., Governor  
SOUTHEASTERN (Ala., Fla., Ga., S. C., and Cuba), Sea Island, Ga., Oct. 16-17; E. Dice Lineberry, M.D., W. C. Blake, M.D., Carter Smith, M.D. (Chairman), Robert Wilson, M.D., and J. J. Centurion, M.D., Governors  
ARIZONA, Tucson, Oct. 28; Leslie R. Kober, M.D., Governor  
NEW JERSEY, Trenton, Nov. 4; Edward C. Klein, Jr., M.D., Governor  
MIDWEST (Ill., Ind., Iowa, Minn. and Wis.), Milwaukee, Nov. 21; Howard Wakefield, M.D., Charles H. Drenckhahn, M.D., J. O. Ritchey, M.D., Wesley W. Spink, M.D., and Karver L. Puestow, M.D., Governors; Francis D. Murphy, M.D., Chairman.  
MICHIGAN, Ann Arbor, Dec. 5; H. Marvin Pollard, M.D., Governor

### 1954

EASTERN PENNSYLVANIA, Philadelphia, Jan. 15; Thomas McMillan, M.D., Governor  
VIRGINIA (city to be selected), Feb. 25; Charles M. Caravati, M.D., Governor  
KANSAS, Topeka, March 19; Wm. C. Menninger, M.D., Governor; Rudolph Chess, M.D., Chairman of Arrangements; D. R. Bedford, M.D., Program Chairman  
SOUTHERN ILLINOIS, Peoria, March; Charles H. Drenckhahn, M.D., Governor; George W. Parker, M.D., Chairman of Arrangements  
NEW ENGLAND (Conn., Maine, Mass., N. H., R. I., and Vt.), Hartford, Conn., Oct. 22; John C. Leonard, M.D. (Chairman), Richard S. Hawkes, M.D., Richard P. Stetson, M.D., Sven M. Gundersen, M.D., Marshall N. Fulton, M.D., and Ellsworth L. Amidon, M.D., Governors

## NORTH CAROLINA TO CONDUCT TWENTIETH ANNIVERSARY REGIONAL MEETING

Twenty years ago Regional Meetings of the College were first initiated in North Carolina. Under successive Governors these meetings have been promoted year after year until their program becomes a model for other regions. One is readily aware of the results of this long continued program when he attends the North Carolina Meeting or talks with a North Carolina Fellow. Loyalty to the College and to other members of the College, interest and cooperation are the characteristics one finds everywhere.

The members in North Carolina will celebrate their Twentieth Anniversary Regional Meeting at Raleigh, December 3, 1953, under the Governorship of Dr. Elbert L. Persons. Dr. Persons is Associate Professor of Medicine and of Preventive Medicine at Duke University School of Medicine and Associate Physician at Duke Hospital. Preparations for the meeting and organization of the program are already going forward. With pride, yet with due humility, Governor Persons and the North Carolina members look forward to a signal celebration, and extend a cordial invitation to members of the College from other states to join them at this meeting.

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FUTURE MEETINGS

## Annual Sessions, American College of Physicians

1954—Chicago, Ill., April 5-9

1955—Philadelphia, Pa., April 25-29

## Clinical Congresses, American College of Surgeons

1953—Chicago, Ill., October 4-9

1954—Atlantic City, N. J., November 14-19

1955—Chicago, Ill., October 30-November 4

1956—San Francisco, Calif., October 6-12

## Annual Meetings, American Medical Association

1954—San Francisco, Calif., June

1954—(Interim Session) Miami, Fla., December

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ACP ELECTION OF MEMBERS

The next meetings of the College Committee on Credentials at which action will be taken on proposals for membership will be held Nov. 13-14, 1953, and Feb. 27-28, 1954. Proposals must be in the Executive Offices sixty days in advance of the meetings of the Committee. College Governors may require that proposals reach them ninety days in advance to allow them thirty days for local investigation.

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COMING EXAMINATIONS BY CERTIFYING BOARDS

The American Board of Pediatrics, John McK. Mitchell, M.D., Executive Secretary, 6 Cushman Road, Rosemont, Pa.

Oral Examinations Miami, Fla., Oct. 9-11, 1953.

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PROGRESS REPORT, ACP INSURANCE PLANS

The Health and Accident Plan qualified as of April 15, 1953, and since that time many additional applications have been filed with the Association Service Office (1500 Walnut St., Philadelphia 2, Pa.) of the College. Newly elected members were given sixty days from date of notification of election in which to enroll in the Plan

without proof of insurability. To the original group of members an extension of time to June 30, 1953, in which to subscribe, was given through the request of the College and its brokers. However, no further extension will be made, and those (except newly elected members) now wishing to enter the Plan will be subject to proof of insurability.

The insurance carrier, Educators Mutual Insurance Company of Lancaster, Pa., retains the right to reduce the amount of benefits from Class A (\$100 weekly) to Class B (\$50 weekly) or Class C (\$25 weekly) in the case of applicants who have unsatisfactory health records, but during the qualifying period, January to June, 1953, did not have the right to refuse coverage (minimum, Class C) to any qualified member of the College under seventy years of age and still in active medical work. The Committee on Insurance of the College will gladly review any case in which a member feels his coverage was improperly reduced by the underwriter.

Already since the Health and Accident Plan went into effect, thirteen claims for disability have been filed and are being promptly serviced. It must be borne in mind that any disability prior to April 15, 1953, the date of the qualification of the Plan, is not covered. Written notice of injury or of sickness upon which claim may be based must be given to the Company within twenty days of the date of the commencement of the loss for which benefits may be claimed. Written proof of loss of time on account of disability for which claim is made must be furnished to the Company within ninety days after the termination of the period for which claim is made. Members should familiarize themselves with all the benefits covered and regulations relating thereto by reading their certificates.

**Professional Liability Plan.** This Plan remains open for participation. The Plan provides protection against malpractice suits and claims. Incidence of claims against physicians has been markedly increasing in recent years, resulting in increased premiums. Many physicians are faced with materially increased rates at the termination of their present policies. The College Plan through Lloyds of London is advantageous in rates in almost every case; the malpractice risk on members of the College is believed to be superior to that for physicians generally; and it is believed will be reflected by increasingly favorable rates if the majority of members join the Plan.

Briefly, the following are causes of claims and are responsible for the rapid increase in the incidence of claims: (a) Claim-minded patients; (b) Getting something for nothing; (c) Failure on the part of the attending physician to respond to the desires of the patient, or to heed his complaints; neglect; resentment at the doctor's attitude or lack of frankness; (d) Unnecessary and ill-advised criticisms by other doctors; (e) Doctor's fees often are considered too high; (f) Doctors' suits to collect fees from dissatisfied patients (they turn around and sue the doctor). (Some of these causes are quoted from Dr. Thomas M. d'Angelo, Chairman of the New York State Medical Association's Malpractice Insurance and Defense Board.)

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#### INCOME TAX STATUS OF POSTGRADUATE COURSE EXPENSES

For the past three or more years the attorney for the American College of Physicians has been following carefully the tax status of expenses for postgraduate courses offered by the American College of Physicians to its members. The Bureau of Internal Revenue has maintained that such expenses are not deductible since the law specifically refers to non-deductibility of personal expenses in which category it has placed the expense of postgraduate education. From a purely practical and non-legal standpoint, the short, intensive courses offered by the College are in essence no different from the Annual Meeting of the College, expenses for which are deductible on Income Tax Returns. Furthermore, the College has maintained that the pursuit of

these courses is a necessary activity of the physician in keeping abreast of medical progress and maintaining his position to perform his duties to his patients adequately.

Our attorney has reviewed a recent test case, which was appealed and the decision of the Tax Court reversed by the United States Court of Appeals for the Second Circuit, a very strong court. The case concerned a lawyer who practiced in a partnership which was engaged in general practice, but required at least one man to be skilled in tax matters. He undertook this responsibility and his partners relied on him to keep well informed on the subject. In 1946 he attended the Fifth Annual Institute on Federal Taxation sponsored by the Division of General Education of New York University, and in so doing incurred expense for tuition, travel, board and lodging of \$305.00, which he claimed as a deduction under Sec. 23 (a) (1) (A) of the Internal Revenue Code as an ordinary and necessary expense of carrying on a trade or business. The Tax Court disallowed the deduction, finding the expenses to be personal in nature (Code Sec. 24 (a) (1)).

In reversing the Tax Court, the Appellate Court seemed careful not to disturb the rule that one might not deduct the expense of acquiring knowledge for its own sake as an addition to one's cultural background or for possible use in some work to be started in the future. Such expenses apparently will remain, under this decision, personal and not deductible. The Court found the expense to be analogous to the expense of dues and subscriptions to professional societies and journals which are deductible under the regulations. The Court also found that the information acquired was needed in the lawyer's established practice and that he was morally bound to keep well informed. Attendance at the institute was, in the opinion of the Court, a way well adopted to fulfill his professional duty to keep sharp the tools he actually used in his going trade or business. Thus the Court seemed to emphasize the tax-lawyer's moral duty to his partners and his professional duty to clients. The Court concluded that the professional need to keep current in order to perform his work over-shadowed any personal benefit in the form of increased general knowledge.

The Court referred to another case, *Norah Hill*, who was a schoolteacher who pursued a postgraduate course in order to retain her teaching license, in accordance with regulations of the Board of Public Instruction. In comparing these cases, the Court could find only the difference in the degree of necessity. *Norah Hill* had to take the course to retain her license. The lawyer in question could have continued in practice without the course, but he was, as noted, both morally and professionally bound to improve his knowledge in some such fashion.

In the opinion of the College attorney, under this latter decision, the expense of attending college and professional schools will continue to be non-deductible, but that expense will be deductible which is incurred by an active practitioner for the purpose of maintaining and improving his professional skill in a changing field.

This is not necessarily a final decision. The case is subject to appeal to the Supreme Court, but that Court may well refuse to review the case since it is not in conflict with decisions in other courts of appeal. If there is no appeal, the Commissioner may issue further rulings in which he may attempt to restrict the case or, as sometimes happens, he may revise all existing rulings and apply the case broadly. In the meantime it is the College attorney's opinion that the law is that practicing doctors attending courses of the American College of Physicians in order to maintain or improve skills used in practice may deduct the cost of so doing in computing net income subject to federal tax. It must be understood, however, that there may be further litigation by the Commissioner of their right to do so.

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#### MAYO CLINIC MAKES DONATION TO ACP POSTGRADUATE PROGRAM

From March 23-27, 1953, a course, entitled "Selected Subjects in Internal Medicine," was given for the American College of Physicians at the Mayo Clinic under the

joint direction of Drs. Edgar V. Allen, Arlie R. Barnes, William H. Dearing, and Hugh R. Butt. Sixty-eight physicians from various parts of the United States and Canada, all members of the College, were in attendance, and many had to be turned away. The proceeds of the course, as usual, were turned over to the directors for local expenses, and there developed a balance of \$339.11, which the Mayo Clinic turned back to the College as a gift to the Postgraduate program.

#### JOINT COMMISSION ON ACCREDITATION OF HOSPITALS

At its meeting on April 19, 1953, in Chicago, the Board of Commissioners of the Joint Commission on Accreditation of Hospitals reviewed the recommendations on surveys of 284 hospitals which had been conducted by field representatives of the American College of Surgeons, the American Hospital Association and the American Medical Association since January 1, 1953.

The Board granted Full Accreditation to 199 hospitals, Provisional Accreditation to 46, and 38 hospitals were not accredited. These hospitals will be informed of their status on or about May 15.

The Board reviewed the recommendations of three committees which had been appointed to consider changes in the standards published in the "Manual of Hospital Accreditation." Two significant revisions in the standards were made, one of which will serve to ease the multiplicity of monthly meetings that medical staff members must attend, while the other clarifies and makes more specific the organization and functions of general practice departments in hospitals. In addition, certain regulations were adopted as an interpretation of the standard requiring safety precautions in X-Ray departments.

**Medical staff meetings:** Hospitals whose medical staffs have been complaining about the need for attending a multiplicity of monthly staff meetings will be pleased to learn of an additional alternative in the standards which will assist in improving the quality of medical care.

Monthly meetings of the medical staff were designed primarily to aid the staff in discharging its full responsibility for establishing and maintaining high quality of medical care in the hospital. Such meetings, therefore, should be devoted to the thorough review and analysis of the professional management of all discharged patients. In recent years, in those hospitals which have departmental organization with well-qualified and highly specialized clinical staffs, importance has been placed on departmental and clinico-pathologic conferences for extensive study of each patient's record. With a program of departmental conferences, meetings of the entire active staff are required quarterly.

It was agreed that the sole reason for requiring staff meetings is to insure good medical care and treatment of patients in hospitals. The discussion centered on the question: "Are medical staff meetings the best method for accomplishing this?"

In this discussion, the following principles were agreed to:

- 1) The medical staff is responsible for the quality of medical care in the hospital and must accept and assume this responsibility, subject to the ultimate authority of the hospital governing board.
- 2) The medical staff must be a self-governing body.
- 3) Staff meetings are held for the purpose of reviewing the medical care of patients within the hospital and not for the presentation of scientific papers or discussions.
- 4) Regular and frequent meetings of departmental staffs to review clinical work are accepted as a "must" in well-organized hospitals.
- 5) Medical staff meetings cannot be held in conjunction with those of another hospital or with local medical societies.

In addition to the present standards, which require a monthly staff meeting with 75 per cent of the active staff in attendance, or in well-departmentalized hospitals where departmental meetings and clinico-pathologic conferences review the clinical work, a quarterly staff meeting is required, the following alternative was adopted to insure a thorough review of the medical care practiced in the hospital:

- 1) An active Medical Records Committee to review the record of every patient discharged from the hospital.
- 2) An active Tissue Committee to study all pathological reports in relation to clinical data.
- 3) An Executive Committee of the medical staff to review and to take action on the findings of the Medical Records and Tissue Committees.
- 4) General staff meetings to inform and to discuss with the entire medical staff the quality of care currently rendered in the hospital.

The approved standard relating to medical staff meetings follows:

#### Section A-2 (6)

- (a) Executive Committee to co-ordinate the activities and general policies of the various departments, to act for the staff as a whole under such limitations as may be imposed by the staff, and to receive and act upon the reports of the Medical Record, Tissue, and such other Committees as the medical staff may designate. The Executive Committee to meet at least once a month and maintain a permanent record of its proceedings and actions.
- (b) Medical Records Committee, to supervise and appraise medical records, and to insure their maintenance at the required standard. Such Committee to meet at least once a month and submit to the Executive Committee a report in writing which will be made a part of the permanent record.
- (c) Tissue Committee, to study and to report to the staff, or the Executive Committee of the staff, the agreement or disagreement between preoperative diagnoses and reports by the pathologist on the tissues removed at operation. Such Committee to meet at least once a month and submit to the Executive Committee a report in writing to be made a part of the permanent record.

#### Section A-2

- (7) Staff Meetings. The sole objective of staff meetings is improvement in the care and treatment of patients in the hospital. Active staff attendance shall average at each meeting at least 75% of the active staff who are not excused by the Executive Committee for exceptional conditions such as sickness or absence from the community. Each active staff member shall attend 75% of staff meetings unless excused by the Executive Committee for exceptional conditions such as sickness or absence from the community. In addition to matters of organization, the programs of such meetings must include a report of the Executive Committee and be limited largely to the review of current or recent cases in the hospital. Scientific programs not associated with the work of the hospital do not meet this requirement.

#### Section B-2

- (4) Staff meetings (a) In hospitals where adequate review of the medical work in the hospital is carried out by the Medical Records and Tissue Committees and appropriate study and action is taken by the Executive Committee on not less than a monthly basis, one meeting of the entire Active Staff must be held during each quarter of the year. At such meetings a report of the medical work of the hospital must be presented by the Executive Committee.

(b) In well-organized and departmentalized hospitals, departmental conferences and clinico-pathologic conferences may be substituted for meetings of the entire staff, provided that all of the medical work of the hospital is covered by one or another of such conferences and further provided that at least one meeting of the entire Active Staff is held during each quarter of the year. At such meetings a report of the review of its medical work of the hospital must be presented by the Executive Committee. The attendance requirement applies at all such meetings (see A 2 a (7), above).

(c) Business or other executive sessions of the staff will be conducted by the Active Staff and other categories of the staff may be excluded.

General Practice Departments: The standard which permits elective General Practice departments in well-departmentalized hospitals was changed to read as follows:

"A Department of General Practice shall be an organized segment of the medical staff comparable to that of other staff departments with the following limitations:

- "1) The responsibilities of this department shall be limited to administration and education. It shall not be a clinical service and no patients shall be admitted to the department. If and when desirable, however, the department may be made responsible for conducting the out-patient clinic in whole or in part.
- "2) Since the Department of General Practice will not have a separate service, the members of the General Practice Department shall have privileges in the clinical services of the other departments in accord with their experience and training, on recommendation of the Credentials Committee. In any service in which any general practitioner shall have privilege, he shall be subject to the rules of that service and subject to the jurisdiction of the chief of the clinical service involved."

#### COLLEGE PARTICIPANTS IN A.M.A. MEETING

Many members of the College contributed to the success of the annual meeting of the American Medical Association, which was held in New York City, June 1-5. In Monday morning's General Scientific Meeting, presided over by Dr. Alphonse McMahon, F.A.C.P., St. Louis, Dr. Tom D. Spies, F.A.C.P., Birmingham, Ala., read a paper on "Pregnancy, Lactation, Growth and Aging as Special Stress Factors on Nutritional Processes"; Dr. Ovid O. Meyer, F.A.C.P., Madison, Wis., spoke on "Treatment of Hodgkin's Disease and the Lymphosarcomas"; and Dr. Henry A. Schroeder, Sr., F.A.C.P., St. Louis, discussed "Medical Management of Hypertension." In the session on Monday afternoon, presentations included those of Dr. F. Raymond Keating, Jr., F.A.C.P., Rochester, Minn., (co-author), "Postoperative Adrenal Insufficiency in Patients Who Have Taken Cortisone Prior to Surgery"; Dr. John Z. Bowers, F.A.C.P., Salt Lake City, "Today's Medicine in Underdeveloped Areas"; and Dr. Elmer L. Sevringhaus, F.A.C.P., Nutley, N. J., "Interdependence of the Medical Profession and the Pharmaceutical Manufacturers." Friday's session included papers by Dr. Bowers on "Atomic Medicine for Tomorrow's Patient" and by Dr. Paul D. White, F.A.C.P., Boston, on "How Can We Protect the Youth of Today Against the Heart Ills of Tomorrow?"

In the meetings of the Section on Internal Medicine, of which Dr. Truman G. Schnabel, F.A.C.P., Philadelphia, was Chairman, Dr. White delivered the Billings Lecture, entitled "The Principles and Practice of Prognosis with Particular Reference to Heart Disease." Dr. Louis N. Katz, F.A.C.P., Chicago, collaborated on the presentation of "Coronary Dilators and Angina: A Reappraisal"; and Dr. A. Carlton Ernstene, F.A.C.P., Cleveland, was one of those opening the discussion. Dr. W. A.

Jeffers, F.A.C.P., and Dr. Charles C. Wolferth, F.A.C.P., Philadelphia, were two of four co-authors of "The Clinical Course of 72 Patients with Severe Hypertension Following Adrenal Resection and Sympathectomy," with Dr. William Dock, F.A.C.P., Brooklyn, N. Y., being one of the opening discussers. Dr. Robert H. Williams, F.A.C.P., Seattle, Wash., began the discussion of "The Use and Misuse of Radioiodine in the Treatment of Cancer of the Thyroid"; and Dr. Carroll M. Leevy (Associate) and Dr. Thomas J. White, F.A.C.P., Jersey City, N. J., were among the collaborators on "Clinical Observations on the Fatty Liver." "Diagnostic Significance of Blood Sugar Findings" was presented by Dr. Christopher J. McLoughlin, F.A.C.P., and Dr. Lester M. Petrie, F.A.C.P., Atlanta, Ga., with Dr. Garfield G. Duncan, F.A.C.P., Philadelphia, being one of those who opened the discussion. Dr. David T. Smith, F.A.C.P., Durham, N. C., was one of two who opened the discussion on "Active Chronic Pulmonary Histoplasmosis," of which Dr. W. D. Sutliff (Associate), Memphis, Tenn., was a co-author. Dr. Richard S. Gubner, F.A.C.P., Brooklyn, and Dr. Harry E. Ungerleider, F.A.C.P., New York, were among the collaborators on "Effect of Monocaproyl Derivative of Diaminodiphenylsulfone (Equityl) in Experimental and Clinical Tuberculosis," with Dr. Benjamin Burbank, F.A.C.P., Brooklyn, the discussor. Dr. Walter L. Palmer, F.A.C.P., Chicago, a Regent of the College, began the discussion of "Acute and Chronic Bacillary Dysentery," of which Dr. William Wolarsky (Associate), New York, was one of the authors. Dr. Paul S. Rhoads, F.A.C.P., and Dr. Carl E. Billings (Associate), Chicago, were among the contributors to the paper on "The Clinical Use of 1-Hydrazinophthalazine and Hexamethonium in the Treatment of Hypertension," which was discussed by Dr. Irvine H. Page, F.A.C.P., Cleveland. The Chairman's Address, delivered Wednesday by Dr. Schnabel, was entitled "Some Reflections on the American Board of Internal Medicine."

The College was also well represented in the various other Sections, with many members making presentations. In addition, Dr. John H. Lamb, F.A.C.P., Oklahoma City, was Chairman of the Section on Dermatology and Syphilology; Dr. Joseph C. Placak, Sr., F.A.C.P., Cleveland, was Chairman of the Section on Diseases of the Chest; and Dr. Richard A. Kern, F.A.C.P., Philadelphia, Secretary-General of the College, presided over the Section on Military Medicine. Dr. Chester S. Keefer, F.A.C.P., Boston, College Regent, delivered the Minot Lecture on "Subacute Bacterial Endocarditis: The Present-Day Treatment," before the Section on Experimental Medicine and Therapeutics; and Drs. Leon Unger, F.A.C.P., Chicago, Oscar Swineford, Jr., F.A.C.P., Charlottesville, Va., and George L. Waldhott, F.A.C.P., Detroit, participated in the Session on Allergy.

#### INSTITUTE ON SPEECH TO BE HELD IN CLEVELAND

An Institute on teaching and improving esophageal speech will be held in Cleveland, Ohio, August 10-16 at The Cleveland Hearing and Speech Center. This Institute, the second one on Voice Pathology, is being sponsored by the American Cancer Society, National Cancer Institute of Institutes of Health, the Office of Vocational Rehabilitation, the Cleveland Otolaryngological Society, the Cleveland Academy of Medicine and the Western Reserve University School of Medicine.

Nationally known surgeons, speech pathologists and lay teachers of esophageal speech will conduct lectures, demonstrations and supervise practice in teaching esophageal speech; fluoroscopic views will be used to facilitate studies of the physiology of esophageal speech.

Surgeons, speech pathologists and lay persons are invited to attend the sessions. Limited registration is necessary. Application should be mailed by July 15 to Warren H. Gardner, Ph.D., Program Chairman, 11206 Euclid Ave., Cleveland 6, Ohio.

Dr. Sara M. Jordan, F.A.C.P., Boston, delivered the annual oration on "Medicine and the Doctor in Word and Epigram" at the annual session of the Massachusetts Medical Society, held in Boston, May 19-21. Out-of-state speakers and their topics included: Dr. Walter C. Alvarez, F.A.C.P., Chicago, "The Art of Disregarding Findings Which Cannot Explain the Symptoms"; Dr. Howard A. Rusk, F.A.C.P., New York, "Medicine's Number One Problem"; Dr. Anthony C. Cipollaro, F.A.C.P., New York, "Cutaneous Manifestations of Systemic Disorders"; and Dr. Kenneth E. Appel, F.A.C.P., Philadelphia, "Putting the Family Back in Medical Education." Dr. Rusk also addressed the New England Society of Physical Medicine, which held its annual meeting at the luncheon of the Section on Physical Medicine; and Dr. Walter Bauer, F.A.C.P., Boston, served as moderator for a panel discussion on arthritis.

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Dr. A. Carlton Ernstene, F.A.C.P., Cleveland, Dr. J. Harvey Black, F.A.C.P., Dallas, Tex., and Dr. Paul A. O'Leary, F.A.C.P., Rochester, Minn., were among the guest speakers at the annual meeting of the Illinois State Medical Society, which convened in Chicago, May 19-22. Their respective topics were "Management of Cardiac Patients in Relation to Surgery, Anesthesia, and Obstetrics," "Do You Need to Know About Allergy?" and "Dermatological Emergencies Seen in General Practice."

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Dr. Hugh R. Leavell, F.A.C.P., Boston, discussing how a family takes care of its health, addressed the meeting of the Georgia Public Health Association in Atlanta, April 22.

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Dr. Irving S. Wright, F.A.C.P., College Governor for Eastern New York, during the last part of May presented the George Alexander Gibson Lecture of the Royal College of Physicians at the University of Edinburgh Medical College, Scotland.

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The Honorable William C. Marland, Governor of West Virginia, has recently announced the following appointments: Dr. Delivan A. MacGregor, F.A.C.P., Wheeling, member, State Board of Health; Dr. George F. Evans, F.A.C.P., Clarksburg, and Dr. Frank J. Holroyd, F.A.C.P., Princeton, members, Medical Licensing Board.

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Dr. Ernest E. Irons, M.A.C.P., Chicago, President of the Board of Directors of the City of Chicago Municipal Tuberculosis Sanitarium, has recently been made a member of the Illinois Medical Society's Fifty Year Club in recognition of his having practiced in Illinois for a half century.

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Dr. Cornelius DeWitt Briscoe, F.A.C.P., for several years College Governor for Panama and the Canal Zone, is returning to his old home, Monroe, Ga., to do referred practice. Dr. Briscoe has spent 38 years in the Canal Zone and Panama. He became a Fellow of the American College of Physicians in 1929, and became its Governor for Panama and the Canal Zone in 1952, but has now resigned because of his return to the United States. Dr. Amadeo Vicente-Mastellari of Ancon, has been appointed his successor as College Governor.

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Dr. Briscoe was one of the founders of the National Medical Association of the Republic of Panama, a past President of the Isthmian Canal Zone Medical Association, and had been associated with the Herrick Clinic and the Panama Hospital since 1922. The Herrick Clinic was founded by Drs. Herrick, James and Reeder in 1915, American doctors who had been pioneering in the Isthmian Canal Zone with Dr. Gorgas. Before leaving Panama, Dr. Briscoe was decorated by the Governor of Panama with the Order of Basco Nuñez de Balboa, with the rank of Commendador,

and he was also decorated by the Government of the Republic of Ecuador in 1934 with the Order of Merit, with the rank of Official.

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Dr. J. C. Geiger, F.A.C.P., Health Officer for the City of Oakland, Calif., has recently been honored by his native state of Louisiana, where he was also educated. He has been commissioned a Colonel on Gov. Kennon's staff and has been made an Honorary Senator of the Louisiana State Senate.

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Dr. Frederick A. Johansen, F.A.C.P., Carville, La., was honored by his community on his 64th birthday, May 10, prior to his retirement May 31 as Medical Officer in Charge, U. S. Public Health Service Hospital (National Leprosarium). State and national figures joined in "A Day to Remember" to thank Dr. Johansen for his 29-year fight against Hansen's Disease, and included among the congratulatory telegrams were those of Dr. Leonard A. Scheele, F.A.C.P., the Surgeon General, U.S.P.H.S., and Mrs. Oveta Culp Hobby, Secretary of the Department of Health, Education and Welfare.

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Dr. Frederick Tice, F.A.C.P., Chicago, a Fellow of the College since 1916 and a former Vice President and Regent, was honored in May by his former colleagues and students. At the request of the Cook County Hospital Internes' Alumni Association, of which Dr. Edmund F. Foley, Sr., F.A.C.P., is President, the library in the new 3-million dollar, 15-story residence hall for internes and resident physicians at Cook County Hospital has been named in his honor. Dedication ceremonies of the library and the building were held May 3.

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Dr. John J. Andujar, F.A.C.P., Fort Worth, was named President-Elect at the annual meeting of the Texas Society of Pathologists, held recently in Houston.

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Dr. Julius H. Comroe, Jr., F.A.C.P., Philadelphia, was recently appointed to a four-year term as a member of the U.S.P.H.S. Pharmacology Study Section.

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Dr. Thomas L. Findley, F.A.C.P., New Orleans, College Governor for Louisiana, has been named a Consultant in Medicine to the Surgeon General of the U. S. Army. Earlier this year Dr. Findley made a tour of Army hospitals in Japan and Korea.

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Dr. Herbert L. Bryans, F.A.C.P., Pensacola, was recently re-elected President of the Florida State Board of Health for the twelfth term.

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Dr. Edgar R. Pund, F.A.C.P., Augusta, has been elected President of the Medical College of Georgia by the Board of Regents of the University System of Georgia. Dr. Pund has been associated with the Medical College since 1923 and has served as Professor and Director of Pathology.

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The California Society of Pathologists paid tribute to their former President, Dr. Alvin G. Foord, F.A.C.P., Pasadena, by holding a dinner in his honor during the semi-annual meeting on May 23 in Los Angeles. Dr. Foord is Professor of Pathology at the University of Southern California School of Medicine and Director of Laboratories at the Collis P. and Howard Huntington Memorial Hospital.

Dr. Herman Beerman, F.A.C.P., Philadelphia, has recently been elected to life membership in The Medical Society for the Study of Venereal Diseases, London.

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Dr. George Blumer, F.A.C.P., San Marino, Calif., formerly College Governor for Connecticut, was elected an Honorary Member of the Connecticut State Medical Society at the annual meeting in April and was praised in an editorial in the May issue of the *Connecticut State Medical Journal*.

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At the Ninth Annual Congress of the American College of Allergists, held recently in Chicago, Dr. Mayer A. Green, F.A.C.P., Pittsburgh, Pa., was elected First Vice President. Dr. Green also participated in a Symposium on Bronchial Asthma in the postgraduate course that preceded the Congress.

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Dr. Wyndham B. Blanton, Sr., F.A.C.P., Richmond, Va., was elected Vice President of the American Academy of Allergy at the annual meeting in Boston, held earlier this year. Dr. Blanton has also been recently appointed to the Editorial Board of the *Bulletin of the History of Medicine*, published by the Johns Hopkins University.

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Dr. W. Edward Chamberlain, F.A.C.P., Philadelphia, has been awarded the Annual Strittmatter Award for 1952. The gold medal and scroll were presented at the scientific meeting of the Philadelphia County Medical Society on April 8. The thirtieth recipient of the award, Dr. Chamberlain is Professor of Radiology at Temple University School of Medicine.

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The 1952 Joseph Goldberger Award in Clinical Nutrition was conferred on Dr. William Henry Sebrell, Jr., F.A.C.P., Bethesda, Md., at the recent annual meeting of the Council on Foods and Nutrition of the American Medical Association. Dr. Sebrell is Assistant Surgeon General, U. S. Public Health Service, and Director of the National Institutes of Health.

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Dr. Kenneth E. Appel, F.A.C.P., Philadelphia, has been appointed, effective July 1, Chairman of the Department of Psychiatry at the University of Pennsylvania School of Medicine. Dr. Appel, who was named President-Elect of the American Psychiatric Association at its recent annual meeting in Los Angeles, is also Professor of Psychiatry in both the University's School of Medicine and Graduate School of Medicine as well as Director of the Clinic for Functional Diseases at the Hospital of the University of Pennsylvania.

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On the occasion of his 60th birthday, Dr. Albert Salisbury Hyman, F.A.C.P., Associate Clinical Professor of Medicine, New York Medical College, was tendered a testimonial dinner at the Harvard Club by his former students and medical associates on April 29. Dr. Hyman who is Director of Medicine at New York City Hospital was presented with the 1953 Annual Award of the Valley Forge Heart Institute and Research Center which carries the citation for outstanding scientific achievement leading to progress in clinical cardiology. The award was given for Dr. Hyman's original research work concerning the electrophysiology of the dying heart and for his invention and development of the artificial pacemaker for cardiac resuscitation.

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Dr. Elwood A. Sharp, F.A.C.P., Detroit, was honored by the Alumni Association of the University of Kansas School of Medicine on June 7, when he received an award for "distinguished service in medicine." Dr. Sharp has been Director of the Depart-

ment of Clinical Investigation of Parke, Davis & Company since 1929 and was graduated from the University of Kansas in 1913, receiving his M.D. from the School of Medicine two years later.

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Dr. David Marine, F.A.C.P., Rehoboth, Del., has been made the recipient of the 1953 Squibb Institute for Medical Research Award of The Endocrine Society. The award, consisting of a certificate and \$2,500, is given annually for meritorious work in the field of endocrinology and was presented to Dr. Marine at the dinner during the annual meeting of The Endocrine Society in New York City, May 30.

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Dr. Elaine P. Ralli, F.A.C.P., New York, was the Woolley Memorial Speaker at the banquet held May 31 in New York during the annual meeting of the American Medical Women's Association. Her subject was "Physiological Disturbances in Patients with Cirrhosis of the Liver and the Treatment of the Disease."

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Dr. Louis H. Bauer, F.A.C.P., Hempstead, N. Y., Dr. Henry Boswell, F.A.C.P., Sanatorium, Miss., and Dr. Edgar R. Pund, F.A.C.P., Augusta, Ga., were among the out-of-state speakers at a seminar sponsored by the Alumni Association of the Medical Department of the University of Alabama and held in Birmingham, May 21-23.

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Seven members of the College participated in the annual seminar on "Recent Advances in Diagnosis and Therapy" sponsored by the Mount Sinai Hospital of Greater Miami and held in Miami Beach, May 21-23. Authors and their presentations included Dr. Chester S. Keefer, Boston, A.C.P. Regent, "Chemotherapy"; Dr. Stewart G. Wolf, Jr., F.A.C.P., Oklahoma City, Okla., "Psychosomatism"; Dr. Jack D. Myers, F.A.C.P., Durham, N. C., "Heart Disease"; Thomas H. McGavack, F.A.C.P., New York, "The Thyroid"; Dr. Alexander B. Gutman, F.A.C.P., New York, "Metabolism"; Dr. I. Davidsohn, F.A.C.P., Chicago, "Hematology"; and Dr. Stefan S. Fajans (Associate), Ann Arbor, Mich., "Endocrinology."

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Dr. Christopher Parnall, Jr., F.A.C.P., Rochester, N. Y., Dr. Edwin L. Rippey, F.A.C.P., Dallas, Tex., and Dr. David T. Smith, F.A.C.P., Durham, N. C., were among the guest speakers at the yearly meeting of the Louisiana State Medical Society, which was held in New Orleans, May 7-9.

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Dr. LeRoy H. Sloan, F.A.C.P., Chicago, President of the College, and Dr. Louis H. Bauer, F.A.C.P., Hempstead, N. Y., were two of the banquet speakers at the ceremonies commemorating the 100th anniversary of the founding of St. Joseph's Hospital, St. Paul, Minn. In the scientific program on May 16-17, Dr. Francis J. Braceland, F.A.C.P., Hartford, Conn., spoke on "Psychiatry and Religion" and Dr. Burgess L. Gordon, F.A.C.P., Philadelphia, on "Women in Medicine."

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At the yearly session of the West Virginia Academy of General Practice, held May 16-17 in Charleston, guest speakers included Dr. O. Spurgeon English, F.A.C.P., and Dr. John H. Willard, F.A.C.P., Philadelphia, and Dr. Paul L. Shallenberger, F.A.C.P., Sayre, Pa. Their respective topics were "Functional Aspects of Gastrointestinal Disease," "Present-Day Treatment of Ulcers" and "4,500 Consecutive Sigmoidoscopic Examinations."

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Dr. Carl V. Moore, F.A.C.P., St. Louis, College Governor for Missouri, in addition to delivering the banquet address, spoke on "Pathogenesis and Treatment of

Iron Deficiency Anemias" and "Newer Concepts of Pathogenesis of Idiopathic Thrombocytopenic Purpura" at the annual meeting of the Tacoma (Wash.) Academy of Medicine on May 23.

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Dr. Lee E. Sutton, Jr., F.A.C.P., Richmond, Va., was one of the guest speakers at the Symposium on Pediatrics, sponsored by the Committee on Medical Education of the West Virginia State Medical Association and held in Beckley on May 20. His subject was "Pediatric Emergencies."

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Dr. H. McLeod Riggins, F.A.C.P., New York, speaking on "How Should Chest Diseases Be Taught?" and Dr. David A. Cooper, F.A.C.P., Philadelphia, discussing "How Is Our Health?" addressed the joint annual meeting of the National Tuberculosis Association, the American Trudeau Society, and the National Conference on Tuberculosis Workers, held in Los Angeles, May 18-22. In the Symposium on the Unhospitalized Tuberculosis Patient, Dr. Herbert R. Edwards, F.A.C.P., New York, spoke on the "Public Health Problem"; Dr. H. Corwin Hinshaw, Sr., F.A.C.P., San Francisco, discussed the "Medical Problems"; and Dr. Arthur B. Robins, F.A.C.P., New York, was one of the co-authors of "Available Data Bearing on These Problems."

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Guest speakers at the annual session of the Pennsylvania Academy of General Practice, held in Bedford, May 22-23, included Dr. Lewis M. Hurxthal, F.A.C.P., Boston, "Adrenal Disorders"; Dr. Frank J. Heck, F.A.C.P., Rochester, Minn., "Blood Dyscrasias"; and Dr. Hugh Montgomery, F.A.C.P., Philadelphia, "Vascular Diseases."

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In addition to Dr. Louis H. Bauer, F.A.C.P., Hempstead, N. Y., out-of-state speakers at the annual meeting of the Medical Society of the State of North Carolina included Dr. Vince Moseley, F.A.C.P., Charleston, S. C., who spoke on "Diagnosis and Treatment of Acute Pancreatitis," and Dr. Burgess L. Gordon, F.A.C.P., Philadelphia, who discussed "Clinical and Physiological Aspects of Emphysema; Diagnosis and Treatment." The meeting was held in Pinehurst, May 10-13.

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Dr. Raymond B. Allen, F.A.C.P., Los Angeles, Chancellor of the University of California at Los Angeles, was the banquet speaker at the annual meeting of the Aero Medical Association, which convened in Los Angeles in May.

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Dr. W. Edward Chamberlain, F.A.C.P., Philadelphia, was Co-Chairman of the Pathology and Radiology Conference that was part of the annual symposium and the Cancer Pathology and Radiology Conference, which was held May 15-16 in Houston and was sponsored by the University of Texas M.D. Anderson Hospital for Cancer Research with the cooperation of the University of Texas Postgraduate School of Medicine.

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"Allergy in Our Times" was the topic used by Dr. M. Murray Peshkin, F.A.C.P., New York, President of the American College of Allergists, when he addressed the yearly meeting of the Southeastern Allergy Association, held May 15-16 in Nashville, Tenn.

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Dr. I. Arthur Mirsky, F.A.C.P., Pittsburgh, Pa., delivered one of the series of lectures on "Understanding Psychosomatic Disorders" on May 13 at the North Shore Health Resort, Winnetka, Ill.

At the Nineteenth Annual Meeting of the Postgraduate Medical Assembly of South Texas, being held July 20-22 in Houston, Dr. Ray F. Farquharson, F.A.C.P., Toronto, College Governor for Ontario, and Dr. Donald S. King, F.A.C.P., Boston, are among the distinguished guest speakers.

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Dr. Edward H. Rynearson, F.A.C.P., Rochester, Minn., Dr. Arthur C. Curtis, F.A.C.P., and Dr. William D. Robinson, F.A.C.P., Ann Arbor, Mich., were among the guest speakers at the annual meeting of the Kansas Medical Society in Wichita, May 5-7. Their respective topics were "Medical and Surgical Treatment of Goiter," "Skin Manifestations of Lipid Diseases" and "Management of Rheumatoid Arthritis."

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Dr. Louis Weinstein, F.A.C.P., Boston, speaking on "What the Practitioner Should Know About Poliomyelitis," and Dr. Seymour J. Gray, F.A.C.P., Boston, discussing "Effect of ACTH and Cortisone on the Gastrointestinal Tract," were two of the guest speakers at the yearly meeting of the Rhode Island Medical Society, held May 6-7 in Providence.

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Dr. Albert F. R. Andresen, Sr., F.A.C.P., Brooklyn, N. Y., presented the A. Walter Suiter Lecture on "Therapeutic Implications of Gallstones" on May 7 in Buffalo during the annual convention of the Medical Society of the State of New York. Dr. I. Davidsohn, F.A.C.P., Chicago, collaborated in a panel discussion on "Present Blood Banking Problems." Other out-of-state speakers and their subjects included Dr. Eugene P. Pendergrass, F.A.C.P., Philadelphia, "X-Ray Therapy in Neoplastic Diseases," and Dr. Willard O. Thompson, F.A.C.P., Chicago, "Obesity: Causes and Treatment."

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At the annual session of the New Mexico Medical Society, held May 7-9 in Albuquerque, Dr. George R. Herrmann, III, F.A.C.P., Galveston, Tex., read a paper entitled "Diagnosis and Treatment of Coronary Artery Disease" and presided at a round-table luncheon discussion.

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On the partial list of distinguished guests who will address the 21st Annual Assembly of the Omaha Mid-West Clinical Society, to be held Oct. 26-29, are Dr. Francis J. Braceland, F.A.C.P., Hartford, Conn., Dr. Grace A. Goldsmith, F.A.C.P., New Orleans, Dr. William S. Hoffman, F.A.C.P., Chicago, and Dr. Lewis M. Hurxthal, F.A.C.P., Boston.

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Dr. David W. Kramer, F.A.C.P., Philadelphia, addressed the Mercer County (N. J.) Medical Society at Trenton on May 13 on the subject, "Advances in Peripheral Vascular Disorders."

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Dr. Howard F. Root, F.A.C.P., Boston, and Dr. Franklin B. Peck, F.A.C.P., Indianapolis, were the principal speakers at the First Annual Meeting of the Florida Clinical Diabetes Association. In addition to addressing an opening meeting following the dinner, they delivered approximately 12 lectures. The meeting, held in St. Petersburg, May 14-15, was conjointly sponsored by the Department of Medicine of the Graduate School of the University of Florida and the Florida State Board of Health.

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Four Fellows of the College were among the guest speakers at the yearly meeting of the Nebraska State Medical Association, which met May 11-14 in Omaha. Speakers and their topics from San Francisco were Dr. Francis W. Pruitt, "Lower

Nephron Nephrosis as Seen in the Korean Casualties and Its Management," Dr. Lowell A. Rantz, "Uses and Abuses of Antibiotics in the Surgery of Trauma," and Dr. George S. Johnson, "Some Problems of Psychiatry." Dr. Edward H. Ryncarson, Rochester, Minn., discussed "Clinical Syndromes Resulting from the Over-and-Under Function of the Adrenal Glands."

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Dr. Morris L. Drazin, F.A.C.P., Maspeth, N. Y., presented a paper on "Glucose Tolerance in Hypertension and Obesity" before the Scientific Sessions of the 13th Annual Meeting of the American Diabetes Association at New York City on May 31. He also addressed the New York Academy of Medicine recently on the same general subject.

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Dr. Louis H. Clerf, F.A.C.P., Philadelphia, speaking on "Tumors of the Neck," addressed a joint meeting of the West Virginia Academy of Ophthalmology and Otolaryngology with the Virginia Society of Ophthalmology and Otolaryngology in Hot Springs, Va., May 5.

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Dr. Sidney C. Werner, F.A.C.P., New York, was one of the collaborators in a panel discussion on "Radioiodine in the Diagnosis and Treatment of Thyroid Disease" that was part of the program of the annual session of the American Goiter Association, held in Chicago, May 7-9.

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Dr. William Dameshek, F.A.C.P., Boston, addressed the staff of the Manchester (Conn.) Memorial Hospital in April, his topic being "Indications for Splenectomy."

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Dr. Carl J. Wiggers, F.A.C.P., Cleveland, was one of two participants in the annual Cardiac Symposium sponsored by the Waterbury (Conn.) Hospital on April 23. The discussion concerned "Physiology and Clinical Aspects of Pulmonary and Coronary Circulation."

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At the Annual Meeting of the American Therapeutic Society, held May 28-31 in New York, Dr. Arthur C. DeGraff, F.A.C.P., New York, acted as moderator for the Symposium on Tobacco. Panel members and their topics included Dr. W. C. Spain, F.A.C.P., New York, "The Allergic Response to Tobacco," and Dr. A. Wilbur Duryee, F.A.C.P., New York, "Vascular Responses to Tobacco." Dr. O. P. Joseph Falk, F.A.C.P., St. Louis, conducted a Symposium on Recent Advances in Medicine. Dr. Frances M. Pottenger, Jr., F.A.C.P., Monrovia, Calif., delivered the presidential address on "Evidences of the Wulzen Syndrome in Human Beings"; his banquet address was entitled "Sixty Years in Medicine."

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At the annual meeting of the American Heart Association's Council for High Blood Pressure Research, held in Cleveland, May 15-16, Dr. Edgar V. Allen, F.A.C.P., Rochester, Minn., and Dr. George E. Wakerlin, F.A.C.P., Chicago, were Chairmen, respectively, of the morning and afternoon sessions on Friday. Friday's program consisted of reports on "Endocrines and Electrolyte and Water Metabolism in Experimental and Essential Hypertension." Dr. Irvine H. Page, F.A.C.P., Cleveland, was moderator for a panel discussion on "Evaluation of Methods of Treatment of Essential Hypertension," and Dr. Irving S. Wright, F.A.C.P., New York, College Governor for Eastern New York and former A. H. A. President, was Chairman of a panel discussion on "The Layman Asks the Doctor about Heart Disease." Dr. E. Cowles Andrus, F.A.C.P., Baltimore, President-Elect of the Association, addressed the final luncheon session on Saturday.

Dr. Simon Dack, F.A.C.P., Dr. Arthur C. DeGraff, F.A.C.P., and Dr. Herbert J. Kayden (Associate), all of New York City, were among the participants in the Third Annual Cardiac Grand Rounds, which were held at St. Mary's Hospital, Waterbury, Conn., April 2.

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Dr. Robert G. Bloch, F.A.C.P., New York, Chief, Division of Pulmonary Diseases, Montefiore Hospital, addressed the luncheon at the annual meeting of the American Academy of Tuberculosis Physicians in New York, May 30. Dr. Robert G. McCorkle, Sr., F.A.C.P., San Antonio, Tex., delivered the presidential address on the question "Has the Diagnosis and Treatment of Tuberculosis Changed in the Past 25 Years?"

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At the annual meeting of the California Medical Association, held in Los Angeles, May 24-28, Dr. Richard A. Kern, F.A.C.P., Philadelphia, Secretary-General of the College, spoke on "The Growing Problem of Suicide"; and Dr. John H. Talbott, F.A.C.P., Buffalo, N. Y., discussed "Sarcoidosis."

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Dr. Gilbert M. Stevenson, F.A.C.P., for a number of years the former College Governor for Panama and the Canal Zone, effective on June 15, 1953, resigned from the Panama Canal Health Bureau, and accepted an appointment at the Veterans Administration Hospital, Augusta, Ga., beginning July 15, 1953. Dr. Stevenson had been Chief of Medical Service at the Gorgas Hospital for several years.

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Dr. Michael A. Rubenstein (Associate), New York City, has been advanced from Associate in Medicine to the rank of Assistant Clinical Professor of Medicine at New York Medical College, and from Adjunct Attending Physician to Associate Attending Physician at Montefiore Hospital.

# MINUTES OF THE JOINT EXECUTIVE SESSION OF THE BOARD OF REGENTS AND BOARD OF GOVERNORS

ATLANTIC CITY, N. J.

APRIL 12, 1953

A combined Executive Session of the Board of Regents and Board of Governors of the American College of Physicians convened at 2:05 P.M. at Convention Hall, Atlantic City, N. J., April 12, 1953, preceding the opening of the Thirty-fourth Annual Session. President T. Grier Miller presided, Mr. E. R. Loveland was Secretary, and the following were in attendance:

## *Officers and Regents:*

T. Grier Miller	President
LeRoy H. Sloan	President-Elect
Walter B. Martin	First Vice President
Charles F. Moffatt	Second Vice President
Paul F. Whitaker	Third Vice President
William D. Stroud	Treasurer
Richard A. Kern	Secretary-General
A. B. Brower	
Alex. M. Burgess, Sr.	
Reginald Fitz	
George H. Lathrope	
Cyrus C. Sturgis	
Marion A. Blankenhorn	
Asa L. Lincoln	
Walter L. Palmer	
Wallace M. Yater	
Edward L. Bortz	
Herbert K. Detweiler	
Harold H. Jones, Sr.	
Howard P. Lewis	
Maurice C. Pincoffs	
Charles A. Doan	Chairman, Board of Governors
George Morris Piersol	Chairman, Committee on Credentials

## *Governors:*

Arless A. Blair, Fort Smith	ARKANSAS
Stacy R. Mettier, San Francisco	CALIFORNIA (Northern)
Benjamin F. Wolverton, Cedar Rapids	IOWA
Thomas Findley, New Orleans	LOUISIANA
*H. Marvin Pollard, Ann Arbor	MICHIGAN
*H. B. Sweetser, Minneapolis	MINNESOTA
Ralph A. Kinsella, St. Louis	MISSOURI
Harry T. French, Hanover	NEW HAMPSHIRE
Edward C. Klein, Jr., South Orange	NEW JERSEY
Elbert L. Persons, Durham	NORTH CAROLINA
Robert B. Radl, Bismarck	NORTH DAKOTA
Herman A. Lawson, Providence	RHODE ISLAND
Robert Wilson, Charleston	SOUTH CAROLINA

\* Alternate.

Ellsworth L. Amidon, Burlington .....	VERMONT
Charles M. Caravati, Richmond .....	VIRGINIA
George H. Anderson, Spokane .....	WASHINGTON
Paul H. Revercomb, Charleston .....	WEST VIRGINIA
*Norman S. Skinner, St. John, N. B. ...	MARITIME PROVINCES
Walter de M. Sriver, Montreal .....	QUEBEC
*Jose Bisbe y Alberni, Havana .....	CUBA
*D. O. Wright, Birmingham .....	ALABAMA
Leslie R. Kober, Phoenix .....	ARIZONA
Lemuel C. McGee, Wilmington .....	DELAWARE
William C. Blake, Tampa .....	FLORIDA
Carter Smith, Atlanta .....	GEORGIA
Richard P. Howard, Pocatello .....	IDAHO
Howard Wakefield, Chicago .....	ILLINOIS (Northern)
J. Murray Kinsman, Louisville .....	KENTUCKY
Richard S. Hawkes, Portland .....	MAINE
R. Carmichael Tilghman, Baltimore ...	MARYLAND
Laurance J. Clark, Sr., Vicksburg .....	MISSISSIPPI
Harold W. Gregg, Butte .....	MONTANA and WYOMING
Walter I. Werner, Albuquerque .....	NEW MEXICO
Irving S. Wright, New York .....	NEW YORK (Eastern)
Karver L. Puestow, Madison .....	WISCONSIN
Rafael Rodriguez-Molina, San Juan ...	PUERTO RICO
David W. Carter, Jr., Dallas .....	TEXAS
John W. Scott, Edmonton .....	ALBERTA and BRITISH COLUMBIA
Charles H. A. Walton, Winnipeg .....	MANITOBA and SASKATCHEWAN
Leland Hawkins, Los Angeles .....	CALIFORNIA (Southern)
Constantine F. Kemper, Denver .....	COLORADO
John C. Leonard, Hartford .....	CONNECTICUT
*J. Lawn Thompson, Washington .....	DISTRICT OF COLUMBIA
Charles H. Drenckhahn, Urbana .....	ILLINOIS (Southern)
James O. Ritchey, Indianapolis .....	INDIANA
William C. Menninger, Topeka .....	KANSAS
Chester S. Keefer, Boston .....	MASSACHUSETTS
Joseph D. McCarthy, Omaha .....	NEBRASKA
Edward C. Reifenstein, Sr., Syracuse ..	NEW YORK (Western)
*George N. Barry, Oklahoma City .....	OKLAHOMA
Thomas M. McMillan, Philadelphia ...	PENNSYLVANIA (Eastern)
Charles H. Marcy, Pittsburgh .....	PENNSYLVANIA (Western)
Charles F. Morsman, Hot Springs .....	SOUTH DAKOTA
Conley H. Sanford, Memphis .....	TENNESSEE
Fuller B. Bailey, Salt Lake City .....	UTAH
Nils P. Larsen, Honolulu .....	HAWAII
Ray F. Farquharson, Toronto .....	ONTARIO
Cornelius DeW. Briscoe, Panama .....	REPUBLIC OF PANAMA and the CANAL ZONE
Harry G. Armstrong .....	UNITED STATES AIR FORCE
George E. Armstrong .....	UNITED STATES ARMY
*Robert A. Bell .....	UNITED STATES NAVY
*Clifton K. Himmelsbach .....	UNITED STATES PUBLIC HEALTH SERVICE
Joel T. Boone .....	VETERANS ADMINISTRATION

\* Alternate.

Secretary Loveland read abstracted Minutes of the last meeting of the Board of Regents and of the last meeting of the Board of Governors, which, by resolution, were approved.

Secretary Loveland then presented the following communications:

- (1) Letters from absent Regents.
- (2) Notification that Dr. Raymond M. Galt, F.A.C.P., Chicago, had been appointed A.C.P. representative on the Education and Registration Committee of the American Association of Medical Record Librarians, in accordance with a resolution adopted by the Board of Regents on November 16, 1952.
- (3) Notification that Dr. Dwight L. Wilbur, Regent, was the official A.C.P. representative at the Inauguration of Mr. Clark Kerr as Chancellor, Berkeley Campus, University of California, March 23, 1953, as appointed by President Miller.
- (4) Notification that Dr. Leland Hawkins, A.C.P. Governor for Southern California, was the official A.C.P. representative at the Inauguration of Dr. Raymond B. Allen, F.A.C.P., as Chancellor, Los Angeles Campus, University of California, March 20, 1953, as appointed by President Miller.
- (5) Notification that Dr. LeRoy H. Sloan, as President, will attend the Annual Meeting and Convocation of the Royal College of Physicians and Surgeons of Canada at Montreal, October 30-31, 1953.
- (6) Notification that Dr. Turner Z. Cason, former A.C.P. Governor for Florida, officially represented the College at the University of Florida's Centennial Celebration at Gainesville, Fla., March 19-21, 1953.
- (7) Notification that Dr. Asa L. Lincoln, Regent, was the official A.C.P. Delegate to the Inauguration of Dr. Buell Gordon Gallagher as the seventh President of the City College of New York, February 19, 1953.
- (8) An invitation from Dr. Louis H. Bauer, F.A.C.P., Secretary-General of The World Medical Association, for the College to send one or more observers to the Seventh General Assembly at The Hague, Holland, August 31-September 5, 1953.  
It was agreed that inasmuch as no Regent or Governor knew of a Fellow who would be in Holland at the time of said meeting, Dr. Bauer be thanked for the invitation, but told that no observers are presently available.
- (9) Notice that the Joint Commission on Accreditation of Hospitals had filed official Certified Accountant's Report on its operations to December 31, 1952, showing a budget of \$70,000.00, expenses of approximately \$45,000.00 and a surplus of \$25,000.00.
- (10) An invitation from Dr. Walter E. Batchelder, Assistant Director, American College of Surgeons, for the American College of Physicians to appoint a Fellow as an adviser to the Committee on Cancer of the American College of Surgeons. By resolution it was agreed that the incoming President shall make such an appointment.
- (11) A report that Dr. Robert F. Loeb, F.A.C.P., New York, N. Y., had been appointed by President Miller and had accepted official A.C.P. representation on the Division of Medical Sciences of the National Research Council, as of July 1, 1953, succeeding Dr. Harold Jeghers, F.A.C.P., of Washington.

PRESIDENT T. GRIER MILLER: "At this time it is necessary that we appoint a new member on the Joint Commission on Accreditation of Hospitals, because the term of Dr. William S. Middleton now expires. Other Commissioners include Dr. LeRoy H. Sloan (1954) and Dr. Alex. M. Burgess, Sr. (1955)."

. . . On motion by Dr. Wallace M. Yater, seconded by Dr. Cyrus C. Sturgis, and unanimously carried, Dr. William S. Middleton was reappointed for a term of three years, until 1956. . . .

PRESIDENT MILLER: "First, under new business, will be the report of the Secretary-General, Dr. Richard A. Kern."

DR. RICHARD A. KERN: "This report is limited to deaths and additional Life Members. Since the last meeting of this Board 33 Fellows and 4 Associates have died, as follows: (Read list of names and dates of death for record in Minutes)."

"Since the last meeting of this Board, the following 80 Fellows have subscribed to Life Membership, making a grand total of 1,133 of whom 114 are now deceased, leaving a balance of 1,019: (Read list of names for record in Minutes)."

. . . Members arose and stood in silent tribute to those who had died. . . .

PRESIDENT MILLER: "We shall now have the report of the Chairman of the Committee on Credentials, Dr. George Morris Piersol."

DR. GEORGE MORRIS PIERSOL: "Dr. Miller, members of the Board of Regents and Board of Governors, the Committee on Credentials combines in this report the results of two meetings, one held at the College Headquarters in Philadelphia, March 7-8, 1953, and the other held at Convention Hall, Atlantic City, April 11, 1953. Those in attendance included Doctors George H. Lathrope, J. Murray Kinsman, Lemuel C. McGee, Robert Wilson, Wallace M. Yater (substituting for Dr. J. Owsley Manier) and George Morris Piersol, Chairman."

"A number of communications were received and reviewed. Actions growing out of these were:

- (1) A recommendation that the Executive Secretary prepare an addendum to be added to the Governors' Handbook, emphasizing that a Governor, in endorsing a candidate for Direct Fellowship, shall include in detail the reasons why he considers the candidate qualified for Direct Fellowship;
- (2) Candidates practicing in suburban communities of large cities may be sponsored by Fellows, either from their local communities, or from the larger center, so long as the sponsors are thoroughly familiar with the character, qualifications and practices of the candidate.

"The Committee on Credentials recommends to the Board of Regents that the election to Associateship on November 16, 1952, of *Dr. Sylvio LeBlond*, of Quebec, Canada, be annulled, in view of his refusal to accept election to Associateship, and his subsequent failure to take up such election.

"The Committee by resolution recommended that from now forward there is to be no approval of candidates for advancement to Fellowship until they shall have fulfilled the requirement of attending at least one Annual Session during their Associate term. The Associate term now has been increased to ten years, and no Associate, under regulations of the Regents, is actually eligible for advancement to Fellowship until he has fulfilled this requirement.

"The Committee recommends to the Board of Regents the reinstatement of the following 3 Associates, for terms extending from April, 1953, to a maximal of April, 1958:

1. Dr. Luther Albert Lenker, Harrisburg, Pa.
2. Dr. Meyer Harold Stolar, Washington, D. C.
3. Dr. Robert George Taylor, Washington, D. C.

"To lay some emphasis on the importance of the regulations governing election to Direct Fellowship, a recommendation was approved by resolution that the following sentence be added to Section 4, Page 9 of the white booklet containing detailed requirements, just preceding the last sentence of Paragraph 1:

'Before the proposal shall be endorsed by the Governor, there should be a consultation relative to merits of the proposal among the proposer, seconder and Governor.'

"At the two meetings of the Committee, the credentials of 145 candidates for Fellowship and 308 candidates for Associateship were reviewed. An analysis of the recommendations of the Committee is as follows:

*Candidates for FELLOWSHIP*

Recommended for advancement to Fellowship .....	82
Recommended for election to Direct Fellowship .....	10.... 92
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Recommended for election first to Associateship .....	4
Deferred .....	49
Rejected .....	0
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	145

*Candidates for ASSOCIATESHIP*

Recommended for Election .....	244
Fellowship Candidates recommended for election first to Associateship .....	4*...248
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Deferred .....	51
Rejected .....	13
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	312
Less: Direct Fellow candidates recommended for Associateship .	4*
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	308

"The Committee on Credentials, therefore, recommends to the Board of Regents the election of 92 candidates to Fellowship and 248 candidates to Associateship, per the duplicated lists that are distributed to you for examination."

PRESIDENT MILLER: "There are a number of recommendations requiring separate action, first being the reinstatement of 3 Associates."

... On motion by Dr. Charles F. Moffatt, seconded by Dr. J. Murray Kinsman, duly put and carried, this recommendation of the Committee was approved. . . .

PRESIDENT MILLER: "Next item is the addition of a sentence to Section 4, page 9, of the Informative College Booklet, as recommended."

... On motion by Dr. Paul F. Whitaker, seconded by Dr. A. B. Brower, put and carried, this recommendation was approved. . . .

... On motion by Dr. Alex. M. Burgess, Sr., seconded by Dr. Irving S. Wright, duly put and carried, the following 92 Fellows and 248 Associates were elected, as recommended: (Names already published in the May, 1953, issue of this journal).

PRESIDENT MILLER: "We now come to the report of the Joint Commission on Accreditation of Hospitals by Dr. LeRoy H. Sloan, A.C.P. Chairman."

DR. LEROY H. SLOAN: "Mr. President: This Commission is the result of a large cooperative effort of the American Medical Association, the American College of Surgeons, the American College of Physicians and the American Hospital Association.

"The Commission is governed through the Board of Commissioners, made up of six members from the A.M.A., six from the A.H.A., three from the A.C.P., three from the A.C.S. and two from the Canadian Medical Association. The budget is divided in accordance with this ratio. The College was the first organization to pay

its bill to the Joint Commission, which enabled the Commission to begin its operations. Mr. President, to date the budget of the College amounts to \$9,450. That was due to a surplus of \$32,000 in the Treasury at the initial organization of the Commission, and I venture that the budget of the College will be approximately \$13,000 a year.

"Dr. Edwin L. Crosby, of Johns Hopkins, is Director of the Joint Commission and your representatives are Dr. Burgess, Dr. Middleton and myself.

"The meetings of the Advisory Committee have been held throughout the year, with a ceremony on December 6, 1952, at the John B. Murphy Memorial to convey the important functions of the College of Surgeons to the Joint Commission. Senator Lister Hill gave the address on that particular occasion.

"The Commission is quartered in Chicago in rooms formerly occupied by the College of Surgeons and which are now on rental by the Commission. The files of the College of Surgeons have been turned over to the Joint Commission. The function of the Commission is the accreditation of hospitals in both professional services and in ancillary services.

"It is estimated that over a period of years eight surveyors of the A.M.A. will be able to visit about 350 hospitals and the College of Surgeons about 200, and that will leave a good many hospitals to be covered by the Joint Commission. Because of this, between 750 and 1,000 can be surveyed each year. The Commission will have its own surveyors in addition to the ones granted.

"What problems are coming up at the present time before the Commission? In addition to the approval or disapproval of hospitals, such questions as 'Shall an internist on a staff be required to deliver a baby in the middle of the night if it happens to be his turn to serve?' Well, I think it is recommended that the internist not deliver the baby.

"In addition to that, such problems as 'Shall the internist fluoroscope patients or be permitted to do radiological procedures on patients?' Right now that is before the Commission, because, of course, in patients who are apt to be burned the hospital must take the responsibility in total measure, so that now before the Joint Commission there comes a recommendation of the College of Radiology that only those approved by the Radiological Department be permitted to fluoroscope patients. The same thing applies to children, and the Academy of Pediatrics is now conferring with the Commission on such things as fluoroscopy of children.

"A chief inquiry at the present time concerns the multiplicity of medical meetings."

PRESIDENT MILLER: "That report requires no action. We shall proceed to the report of the Committee on Insurance, Dr. A. B. Brower, Chairman."

DR. A. B. BROWER: "Mr. Chairman, the formal report of this Committee I expect to give on Tuesday. The Committee this morning reviewed what has been done and what has been accomplished in this insurance program, and I can assure you that the Executive Secretary has had a very big job. He has done it well, and the Committee has concurred in everything that he has accomplished."

PRESIDENT MILLER: "As you know, a year ago a Committee on Membership was appointed, with Dr. Richard A. Kern as Chairman. At the November meeting of the Board of Regents, Dr. Kern reported on the status of College membership of members of the teaching staffs of the medical schools in this country. Those data were prepared by checking the catalogs of the various schools and the material being tabulated in the Executive Secretary's Office. The report revealed that only 56½% of the members of the faculties of these medical schools were Fellows or Associates of the College, leaving 43½% who are non-members. Some of us felt it desirable to find out more about that 43½%, and so a letter was sent to the head of every department of medicine, asking for more detailed data regarding the members of his staff who are not associated with the College. As a result, we can now say that many of those

men, younger ones, are in the process of being proposed for membership. Another group are not regarded as qualified for Fellowship in the College, not only because they haven't been certified, but because in other respects they do not qualify for one reason or another. Some are elderly, and, as a matter of fact, some have died since the publication of the catalog. So that leaves instead of 43½% only about 14% of the teachers in this country who are eligible and qualified for membership in the College, but are not yet members.

"Of this group, there are some who have no interest in College membership; some are full-time workers in fundamental science, they don't want to be associated with an organization of this sort, but there are many who would like to join the College and are not members, simply because no one of us has taken up the matter with them. Many of them, I am sure, would now welcome the opportunity to join, and I think many will be proposed. I think this matter is worth following up, for I believe many of the teaching staff of the medical colleges would like to come into the College during the next year.

"This evening at the Haddon Hall Hotel the Regents and Governors will be hosts at a reception and dinner for those Associates and Direct Fellows who were elected by the Board of Regents on November 16, 1952. The chief objective of this party is to extend a very cordial welcome to new members. All of them have been invited. Unfortunately, many did not reply. We sent out 'R.S.V.P.' invitations to 272 and received 73 acceptances, 55 declinations.

"Now, I wish to present Dr. Hilton S. Read, General Chairman of this meeting, who has done a wonderful job in the way of preparations and arrangements."

DR. HILTON S. READ: "President Miller, Regents and Governors: First, we are greatly pleased you are here. Because of my height you can generally see me in any crowd, and if there is anything you want from Atlantic City call upon me. I have for you here special tickets for the Concert of the Philadelphia Orchestra tonight and also for the entertainment in the Ballroom of the Convention Hall tomorrow night. The Schering Corporation has kindly underwritten the entire expenses of the Concert to the limit of \$10,000.00. The entertainment tomorrow evening, which includes radio, television stars and others, is put on solely by the College.

"We have had a most wonderful experience with this meeting. We have worked before with other organizations, but there is no office in the country equal to that of Mr. Loveland and his staff in Philadelphia."

PRESIDENT MILLER: "I would now like Dr. Charles A. Doan, as Chairman of the Board of Governors, to assume the Chair."

DR. CHARLES A. DOAN: "Last year and the year before the Board of Governors occupied a good deal of time on the meeting similar to the one today. I believe the extension of the Associate term to ten years has been universally accepted favorably, and that with the first year of operation under this idea no one has suggested we go back to the five-year limit. I would like to ask Dr. Carter Smith, Governor for Georgia, if he has a report to make for the Committee appointed last year to deal with some recognition for Officers, Regents and Governors at the end of their respective terms."

DR. CARTER SMITH: "Members of the Boards of Regents and Governors: Your Committee has pondered long the question of what to do with ex-Regents and ex-Governors. We feel that they should be given some consideration, more than they have received in the past, and the opinion has been expressed that some of them felt slighted when 'put on the shelf.' We are offering the following recommendations:

- (1) That they be given the opportunity to secure hotel reservations for the Annual Session through the Executive Secretary's Office, as do the active Governors, Regents and Officers.

- (2) That they be given the opportunity to register at the special Registration Window, as do the present active Governors, Regents and Officers.
- (3) That they be given a certificate, indicating the office held and length of service in this office at the termination of their particular assignment.

"The last recommendation brings up some question of technicality which we hope to solve with Mr. Loveland—and this relates to individuals who have held multiple offices. We have eliminated the thought of having something engrossed on the old certificate. We also realize that to have additional certificates would not be too good, so we are open to additional suggestions from the floor."

CHAIRMAN DOAN: "This part of the report is open for discussion."

DR. REGINALD FITZ: "Mr. Chairman, in times past I have noticed that some of the former Regents or Governors, or Officers, have had their feelings a bit hurt, because they were not made part of the academic procession at Convocations, and I wonder whether it would be worth while to make them welcome to march with the rest of the Regents and Governors to the platform, or is the platform inadequate in size?"

DR. LEMUEL C. MCGEE (A.C.P. Marshal): "My experience is limited to two years. In most cases, I think our platform would be adequate to accommodate retired Governors and Regents in the academic procession. I doubt if there would ever be more than a score. It would add dignity to the procession, and as far as I am personally concerned, the Marshal would be glad to have a space provided for them on the stage. There could be occasions when the stage would be too small, in which case some other arrangement could be made."

PRESIDENT MILLER: "I am a little hesitant to accept this without some further investigation. After all, if all of those who have been Officers and Regents and Governors are included, we might have a rather large number. In some instances, the stage would not be large enough to accommodate any more than we now have. I think it wise to consider this a little further before taking final action."

DR. SLOAN: "I agree with Dr. Fitz in his general ideas, and I know that in Chicago the stage will not be large enough to hold the group that you suggest. However, in keeping with all other Convocations, it seems to me that the past Officers can be assigned special seats in the immediate vicinity of the stage, in order that they may feel that they are still an important part of the College, and I suggest that be given further consideration."

CHAIRMAN DOAN: "These suggestions, I assume, may be used by this Committee for resolution of the problem. It might be from year to year, as facilities are adequate or inadequate, invitations could be issued by the Executive Secretary's Office, depending upon stage facilities. Next year at Chicago facilities might not be adequate, in which case some substitute plan might be used."

DR. BENJAMIN F. WOLVERTON: "Does the Committee expect to make these recommendations applicable on a retroactive basis?"

DR. SMITH: "They would include all of those who are still living; therefore, retroactive."

DR. WALTER L. PALMER: "Are these ex-Officers, ex-Regents and ex-Governors invited to the Sunday evening dinner?"

PRESIDENT MILLER: "I think not, although ex-Presidents are usually invited."

DR. PALMER: "I wonder if that should not be given some consideration? It is awfully important to keep some of these former Officers, Regents and Governors coming and associating with us actively, and that would be a function in which I think they might be most interested."

DR. SMITH: "Will Mr. Loveland estimate roughly how many different individuals would be concerned in this ex-group?"

SECRETARY LOVELAND: "I believe there may be about 175 separate individuals, but I suspect that not more than one-half of them would be able to attend the dinner of the Regents and Governors."

... It was agreed that this report be accepted as an exploratory one, and it was suggested that the Committee further confer with the President and the Executive Secretary and bring back to the Board of Governors and the Board of Regents more specific recommendations for definite action. . . .

CHAIRMAN DOAN: "On behalf of myself and the Board of Governors, I wish to express to Mr. Loveland and his associates our appreciation for the Handbook for Governors, which outlines the functions of a Governor. Certainly I, for one, have felt that this was a very essential thing for the incoming Governors particularly and represents a codification of custom that has come with reference to many of the functions of the Board of Governors.

"Is there any new business to come before this Board at this time?"

... There being no further business, Chairman Doan relinquished the Chair to President Miller, who declared the meeting *adjourned* at 3:30 P.M.

Attest: E. R. LOVELAND,  
Secretary

## MINUTES OF THE ANNUAL BUSINESS MEETING

ATLANTIC CITY, N. J.

APRIL 16, 1953

The 1953 Annual Business Meeting of the American College of Physicians, during the 34th Annual Session, was held on April 16, 1953, convening at 2:00 P.M., in the Convention Hall, Atlantic City, N. J., with President T. Grier Miller presiding.

A quorum was declared, and the Executive Secretary read abstracted Minutes of the preceding Annual Business Meeting, which were approved as read.

The Treasurer, Dr. William D. Stroud, presented the following report, which, by resolution, was approved:

"Mr. President, Masters and Fellows of the College:

"The detailed Statements of Operations of the College for 1952, along with the Certified Public Accountant's report, will be published in an early issue of the *ANNALS OF INTERNAL MEDICINE*.

"During the year 1952 the College added to its General Fund, \$68,411.52; to its Endowment Fund, \$35,519.04, or a total of \$103,930.56.

"The Gross Assets of the College, as of December 31, 1952, amounted to \$989,154.16, divided as follows:

General Fund .....	\$576,555.52
Endowment Fund .....	382,598.64
James D. Bruce Fund .....	10,000.00
A. Blaine Brower Fund .....	20,000.00
	<hr/>
	\$989,154.16

"The College operated wholly within its Budget during the past year. Income exceeded budgetary expectations, whereas expenditures were actually less than the appropriations. The investments of the College are supervised by a competent Investment Counselor and by the Committee on Finance, and are carefully reviewed periodically. As of December 31, 1952, the College held Investments at Book Value totalling \$925,822.12, which, as of March 24, 1953, had a current market value of \$1,061,284.00, or an appreciation of \$135,461.88. The average yield for 1952, based on current market value, rather than book or cost price, was 3.87%, but considerably greater when based on cost.

"The Board of Regents has approved a Budget for 1953 calling for an estimated income of \$356,490.00 and an estimated expenditure of \$295,150.00, leaving an estimated balance of \$61,340.00.

"The financial policies of the College and of the Committee on Finance continue to be conservative at all times.

Respectfully submitted,

WILLIAM D. STROUD, *Treasurer.*"

The Executive Secretary, Mr. E. R. Loveland, presented the following annual report, which, by resolution, was accepted:

"Mr. President, Masters and Fellows of the College: As usual, the report of the Executive Secretary is supplementary to those of the President, the Treasurer and the Secretary-General.

"In addition to the usual and customary activities of the College, your Executive Offices have carried out two rather extensive and time-consuming surveys:

- (1) An analysis of the faculties of approved medical schools in the United States and Canada, with regard to membership in the American College of Physicians, this survey being conducted for the Committee on Membership, and thereafter followed up by President Miller by personal letters to Deans or Chairmen of the Departments of Medicine at the various institutions;
- (2) An extensive survey of Group Health and Accident Insurance and Group Malpractice Insurance, suitable and beneficial to the members of the American College of Physicians, subsequently resulting in the Board of Regents officially approving a Group Plan covering Health and Accident and a Group Plan covering Professional Liability. As you have learned earlier in this meeting, both Plans have qualified, so far as participation of the membership is concerned, and are now in effect.

Although the Board of Regents appointed official Brokers to attend to the installation of these plans, they have required a very material amount of effort and time from the Executive Offices, especially in view of the fact that the adoption of these Plans, conflicted in a measure with private insurance plans, which obviously were in conflict with the interests of individual insurance agents who heretofore have written personal rather than group plans for the doctors of the country.

"The Board of Regents and the Board of Governors of the College have many active Committees to whom the membership should be grateful indeed for their contributions of time and productive work. Every Committee has made its contribution, but the volume of work has been especially large in the case of the Committee on Credentials, the Committee on Postgraduate Courses, the Committee on Fellowships and Awards and the Committee on Insurance.

"The Committee on Advertising and Exhibits likewise has done signal work, not only in connection with our Journal, but in presenting to you at this meeting a fine technical exhibit, representing the leading ethical firms and organizations in the medical field, and may I bespeak your support of this fine technical exhibit and of the exhibitors by urging you to take the time to stop by and inspect the exhibits. These firms usually are not here to sell products, but to promote their services to the College and its members, and your appreciation is measured by them in the degree to which you show your interest by visiting their displays.

"Our Postgraduate Course Program has continued outstandingly successful. The circulation of our journal continues to expand; an increasing number of Fellows have become Life Members; Regional Meetings continue to be a popular and beneficial activity under the Governors in the various States and Provinces; our Research Fellowship and Latin-American Fellowship Programs have continued to be highly productive; the Brower Traveling Scholarships, now increased to two, have been widely sought for by our Associates, and the recipients have been deeply appreciative of the excellent advantages that have accrued to them; a Supplement to our 1951 Directory was published, and an entirely new and revised Directory will be published during 1953. We have never had a more interested and effective Committee preparing the Annual Session program than that headed by Dr. Hilton S. Read for the present Session.

"It has been a privilege to work with Dr. Read and his Committees and with our President, Dr. Miller, and with Regents and Governors during the year. At every step, we have had thorough encouragement, advice and ready coöperation.

"We have just received from the Registration Desk a report that the total registration to this time at this meeting is 4,843, of which 1,057 are ladies.\*

Respectfully submitted,

EDWARD R. LOVELAND, *Executive Secretary.*"

The Secretary-General, Dr. Richard A. Kern, then presented the following annual report of his office:

"Mr. President, Regents, Governors, Masters and Fellows of the College: My report will be limited to certain important matters of particular interest to you.

"*Membership:* Since the last Annual Session of this College, there have been elected 2 Masters, 181 Fellows, 514 Associates, which brings the total membership to the following:

Masters .....	15
Fellows .....	5,535
Associates .....	2,269
Total .....	7,819

"*Life Members:* Since the last Annual Session of this College 110 Fellows have become Life Members, bringing the total to 1,133, of which 114 are deceased, leaving a balance of 1,019.

"*Deaths:* Since the last Annual Session we have lost by death 81 Fellows and 8 Associates. Their names and records appear in the Archives of the College, and their obituaries have been published, or will be published, in the ANNALS OF INTERNAL MEDICINE.

"*Postgraduate Courses:* Hertofores there has been a large degree of collaboration between the Regents' Committee on Educational Policy and the Governors' Committee on Postgraduate Courses. The latter Committee has conducted its affairs so effectively that it has now been largely divorced from the Committee on Educational Policy, which will now turn its attention more forcibly to other educational projects. The first such project will be a systematic collection of the evidences of membership satisfaction or dissatisfaction with the program of the Annual Sessions, to analyze these and submit a report for the guidance of the Consulting Committee on Annual Sessions.

"During 1952, under the direction of the Committee on Postgraduate Courses, 16 courses have been conducted in the United States and Canada, with a registration of 1,101 physicians. There appears to be no diminution in the popularity of this excellent program. Shortly after this Session there will be announced in the ANNALS the program of courses for the autumn of 1953, the spring of 1954 and some of the proposed courses for periods thereafter.

"*Fellowships:* The College has currently working 4 Research Fellows, whose program will be concluded on June 30, 1953, and it has awarded 7 additional Research Fellowships for the period July, 1953, through June, 1954. However, two of these

\* Final Registration:

Members .....	2,316
Guest Physicians .....	1,057
Guest Non-Physicians .....	43
Students .....	15
Exhibitors .....	484
Ladies .....	1,063
	4,978

recipients turned back their awards, because they accepted grants through other sources. The programs of 2 previous recipients were interrupted by military service, but will be resumed on July 1 of this year. The work of these Research Fellows is carefully observed with a view to evaluating the program and to act as a guide in the future.

"The College also has 19 Latin-American Fellows presently working in this country, this program being carried on in cooperation with the W. K. Kellogg Foundation, which provides the funds. The program provides an opportunity for the training of Latin-American young men for careers of teaching and research in their homelands. Our Committee on Fellowships has been aided materially through the cooperation of competent and outstanding men who have acted as Preceptors.

"Also during the present year the College awarded 2 Brower Traveling Scholarships to Associates of the College, for the purpose of providing an opportunity to spend a month or more as visiting fellows at some institution, or institutions, for observation, contacts and postgraduate study.

"*Regional Meetings:* During the calendar year 1952, there were 24 Regional Meetings in the United States, Canada and Cuba, with a gross attendance of 2,875 physicians. Already since January 1, 1953, 9 Regional Meetings have been concluded, with nearly 1,000 physicians participating. Regional Meetings are a program of the Board of Governors and fulfill an important purpose in the regional areas of the membership.

"Of greatest significance to the membership-at-large is the Annual Session of the College. This Session in Atlantic City, first in this city and first in its general character, is a further outstanding example of the accomplishments of a year's co-ordinated effort. We are mindful and appreciative of the efforts and accomplishments of those who have made this, the 34th Annual Session of the College, a signal success.

Respectfully submitted,

RICHARD A. KERN, *Secretary-General.*"

. . . By formal resolution, the report of the Secretary-General was accepted. . . .

DR. KERN (continuing): "President Miller, you have served this College faithfully and well in various posts, culminating in its highest office, the Presidency. Under your efficient, constructive and farsighted leadership, the College has progressed to new heights of usefulness, not only to its own membership, but to the cause of medicine, medical education and the medical profession at large. At the same time your genial personality and persuasive manner have gained you the affection and loyal support of all who have been privileged to serve with you. It is, therefore, a particular pleasure to present to you on behalf of the Fellows, Masters, Governors, Regents and Officers of the American College of Physicians the Gavel of your Presidency as a token of our appreciation and as a reminder of our affection and esteem."

(Applause, as presentation was made.)

PRESIDENT T. GRIER MILLER: "Dr. Kern, I greatly appreciate the sentiments that you have expressed on behalf of the Officers, the Regents, the Governors and the Fellows of the College—particularly this material evidence of their regard. It has been a privilege and a great pleasure to work closely with so many of you, and with our efficient Executive Secretary, during the past year. I am deeply grateful for the advice and unfailing support that I have received constantly from all of you. If any advance in the prestige and service of our College has taken place during the period, primary credit goes to my associates. It has been a very happy year for me.

To all of you, let me say that I regard my Presidency in this College as the highest honor that has come to me during my professional career.

"May I ask Dr. LeRoy H. Sloan to come forward?"

"I now wish to present your new President, Dr. LeRoy H. Sloan. His elevation to this high office is a natural consequence of the many and significant services that he has rendered our College. As a Fellow, a Governor, a Regent and finally as President-Elect, he has consistently and ably labored for the accomplishment of the ideals and the objectives of this College. As Chairman of its Conference Committee on Graduate Training in Medicine, of its Committee on Public Relations and of its Committee on the Joint Commission for the Accreditation of Hospitals, his contributions to the welfare of the College have been outstanding.

"With such a background of service, we may be sure that as its President, Dr. Sloan will do much to advance the activities and the prestige of the College during the coming year. I extend to him my personal congratulations and assure him of the affection and support of the entire Fellowship of this College."

(The audience arose and applauded as Dr. Sloan assumed the Chair.)

PRESIDENT LEROY H. SLOAN: "Dr. Miller, I don't know of any one from whom I would rather accept this honor than from you. You have been a devoted servant of the College over a long period of time and have done a fine job. If I can do as well as you have done this year, I shall feel very happy indeed.

"As your President, I shall do the best job I possibly can, and I hope when you come to Chicago next year there will be a good program, good panels and good sessions; that you will enjoy yourself to the fullest.

"My first official function is to submit for the approval of the Fellows and Masters of the College the recommendations of the Board of Regents concerning certain Governorships, in accordance with Article IV, Section (1) of the By-Laws.

"The Board of Regents recommends to you that due to the increase in membership, the Province of British Columbia, Canada, shall have its own Governor, instead of being combined with the Province of Alberta. Also, that the State of Nevada, due to its very small membership, be combined under the Governorship of Northern California."

. . . On motion by Dr. Wallace M. Yater, duly seconded, put and carried, this recommendation was approved. . . .

PRESIDENT SLOAN: "I shall next call on Dr. Walter L. Palmer, Chairman, to make the report of the Committee on Nominations."

DR. WALTER L. PALMER: "President Sloan, Fellows and Masters of the College: As provided by the By-Laws, ex-President Miller appointed a Nominating Committee, consisting of two Regents, two Governors and one Fellow-at-Large. On behalf of that Committee, consisting of Dr. Paul F. Whitaker and myself, Regents, and of Dr. Ray F. Farquharson and Dr. Leslie R. Kober, Governors, and of Dr. A. McGehee Harvey, Fellow-at-Large, I would like to present the following names for the Elective Officers of the College:

<i>President-Elect</i> .....	Dr. Cyrus C. Sturgis, Ann Arbor, Mich.
<i>First Vice President</i> .....	Dr. George F. Strong, Vancouver, B. C.
<i>Second Vice President</i> .....	Dr. Alex. M. Burgess, Sr., Providence, R. I.
<i>Third Vice President</i> .....	Dr. William C. Chaney, Memphis, Tenn."

PRESIDENT SLOAN: "You have heard the report of the Nominating Committee. Are there any nominations from the floor?"



PRESIDENT SLOAN: "You have heard the nominations of Governors by the Nominating Committee. Are there further nominations from the floor?"

. . . There being no further nominations, a motion was made, duly seconded, put and carried, providing that nominations be closed and the Secretary cast a unanimous ballot for these candidates. . . .

PRESIDENT SLOAN: "The candidates for Governorships are declared duly elected. "It is now my pleasure to appoint Dr. Thomas Findley and Dr. Wallace M. Yater to escort the new President-Elect to the platform."

(Applause, as President-Elect Cyrus C. Sturgis was escorted to the platform.)

PRESIDENT SLOAN: "Gentlemen, your new President-Elect."

PRESIDENT-ELECT CYRUS C. STURGIS: "President Sloan, members of the College, first let me express to you my most sincere appreciation for the honor you have accorded me. I am deeply grateful. Let me pledge to you at this time that I shall do all in my power to fulfill the duties of the President-Elect and to try to attain the high efficiency displayed by my illustrious predecessors. Thank you very much."

(Applause.)

PRESIDENT SLOAN: "Dr. Sturgis, I don't know of any one I would rather accept the honor from than Dr. Miller, nor do I know of any one I would rather turn the office over to at the end of my Presidency.

"Newly-elected Governors who have not served previously, or other Governors who may be interested, are invited to meet immediately after this afternoon's Session in the Regents-Governors meeting room with the Chairman of the Committee on Credentials, the Chairman of the Board of Governors, the President of the College and the Executive Secretary.

"I also have to announce that the 1954 Annual Session of the College will be held in Chicago, April 5-9. Chicago welcomes you and is going to give you a good session.

"Dr. Yater, will you now present the resolution of thanks?"

DR. WALLACE M. YATER: "I offer the following resolution of thanks:

"To our distinguished leader and President, Dr. T. Grier Miller, for the inspiration of his guidance during the past year and for the superior program of Morning Symposia and General Sessions at this meeting;

"To his Chief of Staff, General Chairman Hilton S. Read, for the organization of this meeting and for his part of the magnificent program;

"To the Assistant General Chairman, Dr. Clarence B. Whims, and to the Chairmen of the local Atlantic City Committees:

"Dr. Sloan G. Stewart, Chairman of the Committee on Auditorium

Dr. Harold S. Davidson, Chairman, and Dr. Peter A. Herbut, Co-Chairman of the Committee on Clinical-Pathological Conferences

Dr. Robert B. Durham, Chairman of the Committee on Entertainment

Dr. Clarence L. Andrews, Chairman of the Committee on Hotels

Dr. Clifford K. Murray, Chairman, and Dr. Louis B. Laplace, Co-Chairman of the Committee on Panel Discussions

Dr. D. Ward Scanlan, Chairman of the Committee on Publicity

Dr. Matthew Molitch, Chairman, and Dr. Kendall A. Elsom, Co-Chairman of the Committee on Televised Clinics

Dr. Samuel L. Salasin, Chairman of the Committee on Transportation,

and to the individual members of each of those Committees;

"To Mrs. Clarence B. Whims, Chairman of the Committee on Ladies' Entertainment, her assistant, Mrs. Hilton S. Read, and all of their worthy and capable colleagues;

"To the Schering Corporation for making it possible for us to have the pleasure of having a glorious concert by the great Philadelphia Orchestra under the direction of Dr. Eugene Ormandy;

"To Mr. A. H. Slean, Manager of the Atlantic City Convention Bureau, and to his assistants;

"To all of these and many others, individually and collectively, our heartfelt thanks again for their manifold contributions to the success of this memorable meeting and for their most generous hospitality."

PRESIDENT SLOAN: "You have heard the resolution. Is there a second?"

. . . The motion was seconded by many, put and carried. . . .

PRESIDENT SLOAN: "We certainly extend our thanks, as outlined in this resolution, in most hearty form. The hospitality that has been exhibited here in this City has been beyond description. I now declare this meeting officially adjourned."

Adjournment 2:45 P.M.

Attest: E. R. LOVELAND,  
*Secretary*

## OBITUARIES

## COLONEL WESLEY C. COX

Col. Wesley Cintra Cox, (MC), USA, F.A.C.P., died in Richmond, Va., May 22, following a cerebral hemorrhage. At the time of his death, Col. Cox was Commanding Officer of the Army Environmental Health Laboratory at the Army Chemical Center, Edgewood, Md. He was on leave when stricken.

Born in New York City, April 21, 1891, Col. Cox graduated from Columbia University (A.B., 1913) and from the College of Physicians and Surgeons (M.D., 1916). Subsequently he took graduate training at the Army Medical School, Washington, D. C., and Johns Hopkins University (Doctor of Public Health, 1940).

Col. Cox began his Army career in 1917 when he joined the Medical Corps Reserve as First Lieutenant. The following year he was commissioned First Lieutenant in the Regular Army.

During his 36 years of service he held posts as Chief of the Laboratory, Camp Jackson, S. C. (1921), Epidemiologist, Fort Dix, N. J. (1921-22), Serologist and Chief, Laboratory, Eighth Army Area (1926-31), Chief, Laboratory and Medical Inspector, Fort Leavenworth, Kans. (1931-34). Between other assignments, he was Bacteriologist and Instructor (1917-21) and Bacteriologist, Serologist and Instructor (1925-26) at the Army Medical School and Bacteriologist and Instructor, Walter Reed General Hospital (1934-37).

A number of years of service were spent in the Panama Canal Department, where he began his first tour of duty as Bacteriologist in 1922. Leaving in 1925 he returned in 1939 to spend seven more years in the Canal Zone, first as Medical Inspector (1939-42), then Assistant Department Surgeon (1942-43) and finally as Surgeon (1943-47). His other chief post outside of the United States was as Assistant Surgeon, Headquarters, Caribbean Command (1946).

The connection of Col. Cox with the Army Chemical Center dates from 1946, when he was called to head the Industrial Hygiene Laboratory, now the Army Environmental Health Laboratory, a post in which he remained until his death.

Col. Cox had been a Fellow of the American College of Physicians since 1927 and was a member of the American Medical Association, American Public Health Association and the American Geriatrics Association. He was certified by the American Board of Preventive Medicine and held memberships in the American Society of Tropical Medicine and Hygiene, American Association of Industrial Physicians and Surgeons, American Association of Industrial Hygienists, and Association of Military Surgeons. He was awarded the Legion of Merit by the Caribbean Defense Command, October 5, 1945, for his work on sanitation and disease control in that area, and the Army Commendation Ribbon on April 27, 1943, for his health-education activities in schools of the Canal Zone in 1943. In 1946 he was honored by the President of Panama with the Order of Vasco Nunez de Balboa, Grade of Commander.

Department of the Army  
Office of the Surgeon General

## DR. JAMES K. HOWLES

Dr. James Kirby Howles, F.A.C.P., age 55, died suddenly at his home on April 2, 1953.

Dr. Howles was born in Memphis, Tenn., Jan. 6, 1898. Following his elementary schooling in Memphis, he served as a private in the United States Army in France during World War I. He received his B.S., B.M., and M.D. degrees from the

University of Cincinnati and the degree of Master of Medical Science in Dermatology and Syphilology from the University of Pennsylvania in 1932.

In 1932 Dr. Howles became Head of the Department of Dermatology and Syphilology at the Louisiana State University School of Medicine. He developed the department to its present high level of graduate and postgraduate teaching and always worked untiringly for the school in other capacities as well. He was in large measure responsible for the establishment of a three-year residency program in dermatology and syphilology at the Charity Hospital of Louisiana in New Orleans. As Chief of the Louisiana State University Unit in Dermatology at the Charity Hospital, he was responsible for training the majority of the young men in this area presently practicing his specialty.

Dr. Howles carried the burden of an enormous private practice but still found time for teaching, considerable writing and active participation in the staff activities of most of the local hospitals. His textbook on syphilis is one of his outstanding accomplishments.

He was a member of most of the local and national specialty societies and shortly before his death had been elected to the American Dermatological Association. He had been a Fellow of the American College of Physicians since 1940.

In spite of an unbelievably heavy schedule, he always had time to aid others. Dr. Howles was a loyal and friendly colleague and was respected and loved by the profession at large, as well as by those engaged in the practice of his specialty. He will be greatly missed in New Orleans as one of its leading practitioners of medicine.

THOMAS FINDLEY, M.D., F.A.C.P.,  
Governor for Louisiana

#### DR. CHRISTIAN B. LUGINBUHL

Christian Bateman Luginbuhl, M.D., F.A.C.P., Des Moines, Iowa, died January 16, 1953, of adenocarcinoma.

Dr. Luginbuhl was born in Allen County, Ohio, on January 5, 1883. He received his B.S. degree from the University of Chicago in 1912 and graduated in medicine from the Rush Medical College in 1914. He was an Intern in the Presbyterian Hospital of Chicago from 1914 to 1916 and a Resident at Mercy Hospital in Chicago in 1916. In 1916-17 he was a Special Assistant to the American Ambassador to Germany and was detailed, as a Captain in the Medical Corps of the United States Army, to inspect prison camps and hospitals in that country. Following his Army service, he came to Des Moines where he was Attending Physician at the Iowa Methodist Hospital from 1918 and subsequently was Attending Physician at the Lutheran Hospital, Broadlawns Polk County Hospital and Mercy Hospital.

He was a member of the Des Moines Academy of Medicine, the Polk County Medical Society, the American Medical Association, American Association for the Study of Goiter, Tri-State Medical Association, Interstate Postgraduate Medical Association of North America, Iowa Heart Association and the American Association of Railroad Physicians. He was a Diplomate of the American Board of Internal Medicine and a Fellow of the American College of Physicians since 1930. He was a member of Alpha Kappa Kappa fraternity.

Dr. Luginbuhl was an outstanding and respected member of the medical profession in Iowa, and his passing is a distinct loss to his community and to the State.

W. M. FOWLER, M.D., F.A.C.P.,  
Governor for Iowa

## DR. WYMAN RICHARDSON

Wyman Richardson, a Fellow of the College since 1930, died in Boston, February 1, 1953, of thrombosis of the basilar artery. He was in his 57th year. Being a man of strong opinions, ardent enthusiasms and large proportions, his absence is as if one of the rugged lighthouses had suddenly disappeared from his own New England coast.

Wyman was born August 3, 1896, to Dr. Maurice Howe Richardson and Margaret White (Peirson) Richardson of Boston. He early became a lover of nature. As a child he waited through the long winters on Beacon Street for his family's summer migration to Marion on Buzzards Bay. During his school years at Nobel and Greenough, his father and uncles bought a camp on Great Pond at Eastham, and later an old Cape Cod farmhouse on the Eastham Marsh. Here the children were often taken on hunting and fishing expeditions, and here young Wyman became an adept with the rod, the tiller and the fowling piece. It meant a day's journey on the train, then being met at the depot by the wagon and a slow ride around the shore of the Salt Pond while sleepy young eyes watched the sand spill down from the wagon wheels in the flicker of John Sparrow's lantern. These things Wyman loved, and they remained among the happiest memories of his later years.

In 1913 he entered Harvard, perhaps already with the resolve of going on to Medical School, for the medical influence was strong at home; but in April, 1917, the European War reached America, and the call of Plattsburg Officers Training Camp became too strong to resist. Lt. Richardson was assigned to Co. L, 47th Infantry, Fourth Division, fought in the Saint-Mihiel and Meuse-Argonne offensives, and on September 27, 1918, near Montfaucon, he was wounded while directing the fire of his platoon against enemy machine-gun nests. After months of Carrell-Dakin irrigations in Army hospitals, he was disgusted with medicine in all its forms; and on release from the Army, he decided to be a writer. However, when his short stories and essays left the publishing world unmoved, he reluctantly considered going into business and even went so far as applying for a job he did not want. Luckily, he later felt, the head of the chemical firm did not want him either, so his uncle, Frank Benson, took him salmon fishing in New Brunswick. That September Wyman entered Harvard Medical School in spite, as he says, of his brother Edward's scurrilous observation that the motive was really four more Christmas vacations to shoot ducks on Eastham Marsh.

He graduated cum laude in 1923 and became a medical interne at the Massachusetts General Hospital. An even more important event was his marriage on August 19, 1922, to Charlotte Blake Richardson. Married life began in an apartment on Beacon Hill near the Hospital; but shortly after the birth of young Wyman Jr. in 1924, the Richardsons bought a house on Dudley Road in Newton, and Wyman became Assistant in Medicine at the School and Assistant Physician to Outpatients at the Hospital. Thus, by 1928 all the main factors of his life were established—his medicine, his teaching, his family, his home and his hobbies of fishing, shooting, ornithology, writing, and enjoying the company of his friends, particularly at the Farmhouse.

During the next twenty years, Wyman practiced medicine, taught at the School and rose to important positions in the Hospital. He took a particular interest in the use of the blood smear in clinical medicine, and wrote a manual which is still in use at the Massachusetts General Hospital, as well as numerous papers on a variety of medical subjects. Although his principal work was centered around the Massachusetts General Hospital, he also held staff positions at the Eye and Ear Infirmary, McLean, Palmer and Sturdy Memorial Hospitals.

The recent war years made great demands on Wyman's strength. He helped organize the Massachusetts General Hospital unit (Sixth General Hospital), but his application for a commission was rejected because of a spinal fusion. In spite of frequent illnesses, he was active throughout the war as Chairman of a Medical Advisory Board for Selective Service Director of the Baker Laboratory, teacher of special courses in the accelerated program of the Medical School, and he redoubled the intensity of his usual work wherever the war had left things shorthanded. By the end of 1947 his health forced him to give up private practice, but he hoped to continue his teaching and hospital work until he reached retirement age. He soon realized, however, that without the daily stimulus of practice he would be unable to maintain the high standard of teaching he had set for himself and stay in close enough touch with the problems of the hospital staff to fulfill his duties on the General Executive Committee to his own satisfaction. Therefore, in 1949, he retired completely and became a member of the Board of Consultation. Meanwhile his four children, Wyman Jr., Charlotte, Fred and Margaret, had grown up and finished college.

After retiring, Wyman's old interests in Eastham, ornithology and writing stood him in good stead, as did his non-medical clubs, particularly the Tavern and The Nuttall Ornithological Club. Several of his essays on nature appeared in the *Atlantic*, and his article on "Animal Intelligence" is in the *Encyclopedia Yearbook*. He wrote two children's books and four mystery novels with a delightful Cape Cod background and flavor and was revising them for publication at the time of his final illness. He lived to see one of his sons married, but during the wedding festivities he suffered what he thought was a minor heart attack and entered the hospital once more as a patient. Here, among his old students and lifelong colleagues, in the hospital of which he was so proud and for which he had done so much, he died after a short illness.

By his students Dr. Richardson will always be remembered with awe and affection as a brilliant and sometimes imperious but always humble and honest teacher. His colleagues will remember him as a talented diagnostician and painstaking clinician. His intimate friends will treasure the unique charm of days spent with Wyman on the Eastham Marsh and evenings before the Farmhouse fire. A magnetic personality with a deep sense of tradition, Wyman Richardson enriched everything he touched with something of his own coloring and left unforgettable memories in the hearts of all who knew him.

HORATIO ROGERS, M.D.



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1. Greenhill, J. P.: *Principles and Practice of Obstetrics*, ed. 10, Philadelphia, W. B. Saunders Company, 1951, pp. 103-104; 311; 332.

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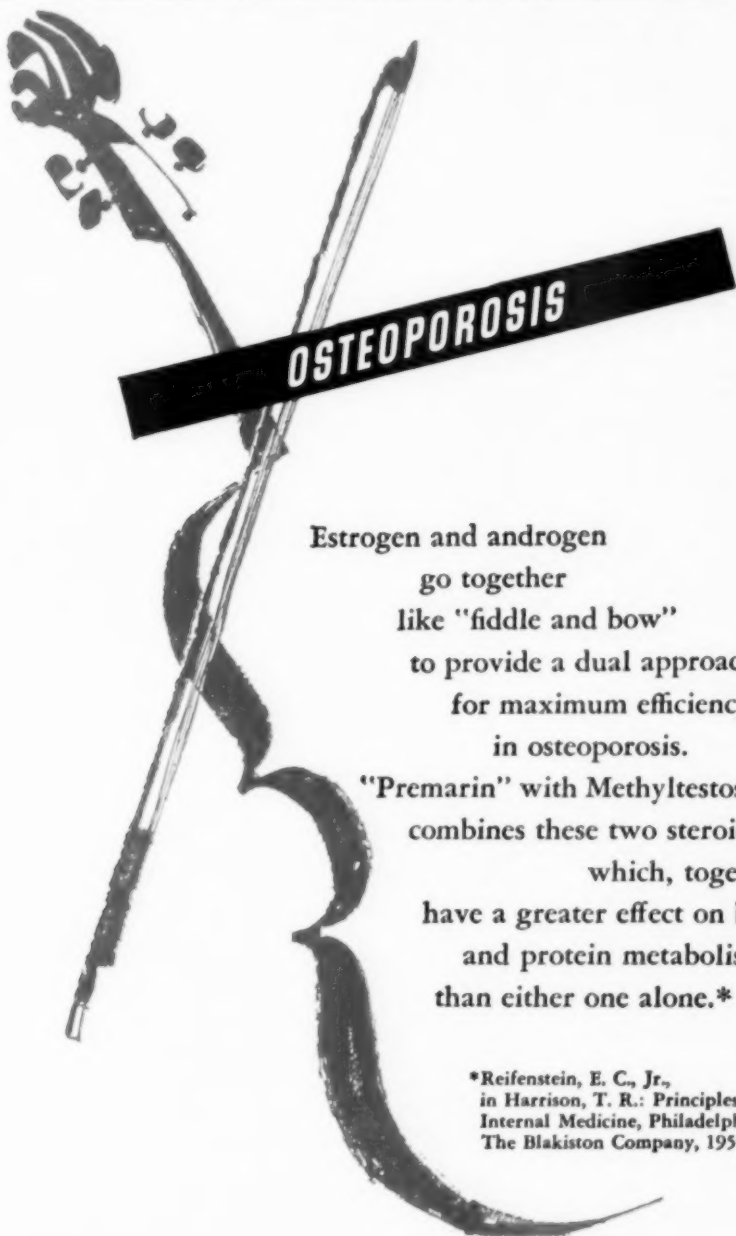
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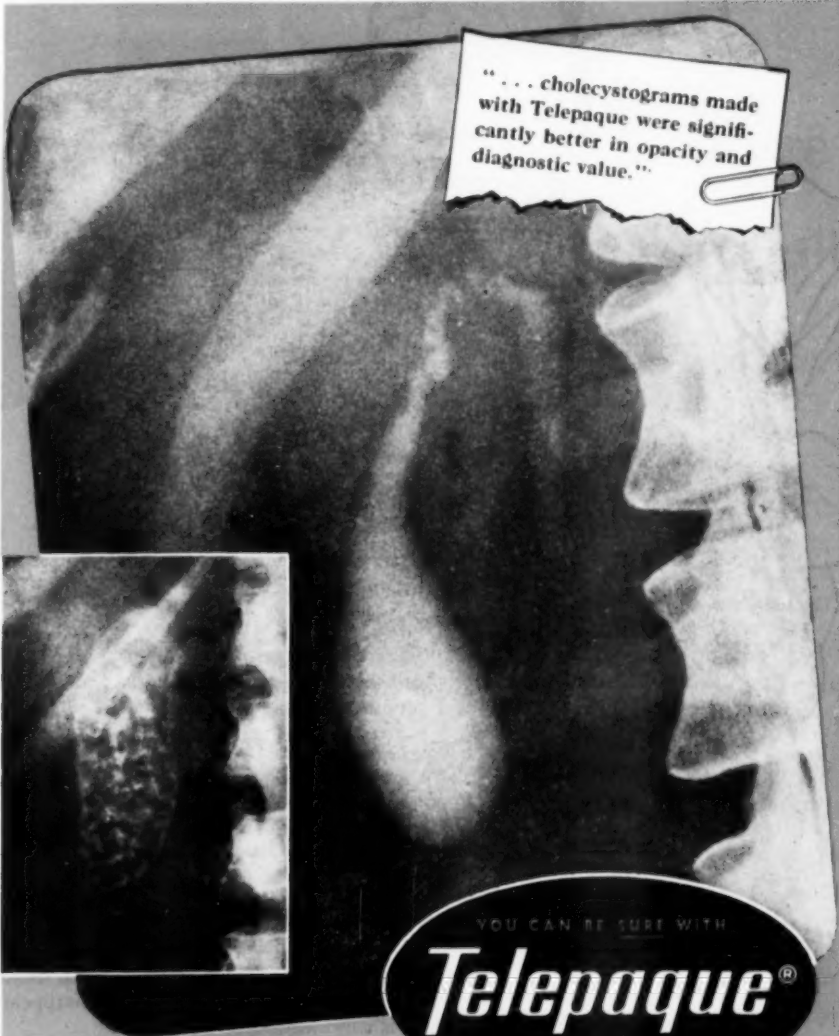
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No.	Course	October		November			December			January 1954						
		5-10	12-17	19-24	26-31	2-7	9-14	16-21	23-28	A.M.A. Interim Session, St. Louis—Nov. 30-Dec. 5	7-12	14-18	21-26	28-Jan. 2	4-9	11-16
1.	<b>CARDIOVASCULAR DISEASES:</b> New York University College of Medicine, New York, N. Y.; Charles E. Kossmann, M.D., F.A.C.P., Director		X						26-28							
2.	<b>PHYSIOLOGICAL BASIS OF INTERNAL MEDICINE:</b> Duke University School of Medicine, Durham, N. C.; Eugene A. Stead, Jr., M.D., F.A.C.P., Director		12-16	19-23												
3.	<b>INTERNAL MEDICINE:</b> University of Chicago School of Medicine, Chicago, Ill.; Wright R. Adams, M.D., F.A.C.P., Director															
4.	<b>CLINICAL NEUROLOGY:</b> Jefferson Medical College of Philadelphia, Philadelphia, Pa.; Bernard J. Alpers, M.D., F.A.C.P., Director					2-6	9-13									
5.	<b>PRESENT DAY THERAPY AND ITS PHYSIOLOGIC BASIS:</b> University of Utah College of Medicine, Salt Lake City, Utah; Maxwell M. Wintrobe, M.D., F.A.C.P., Director															
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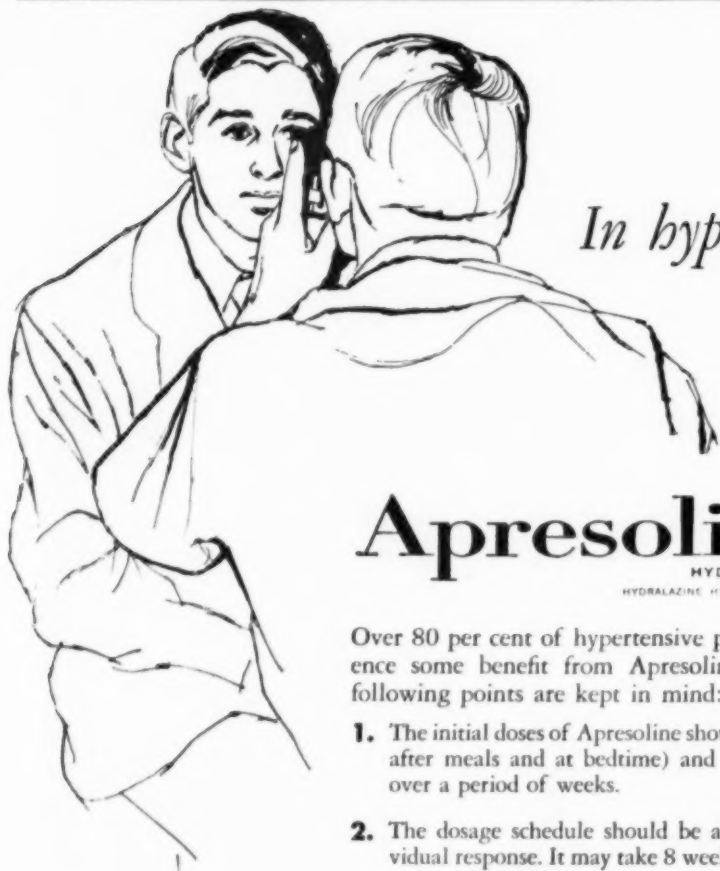
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2. Lawrence, H.M., and Harvey, G.W.: *Connecticut Med. Jour.*, 14:299, Aug., 1950.  
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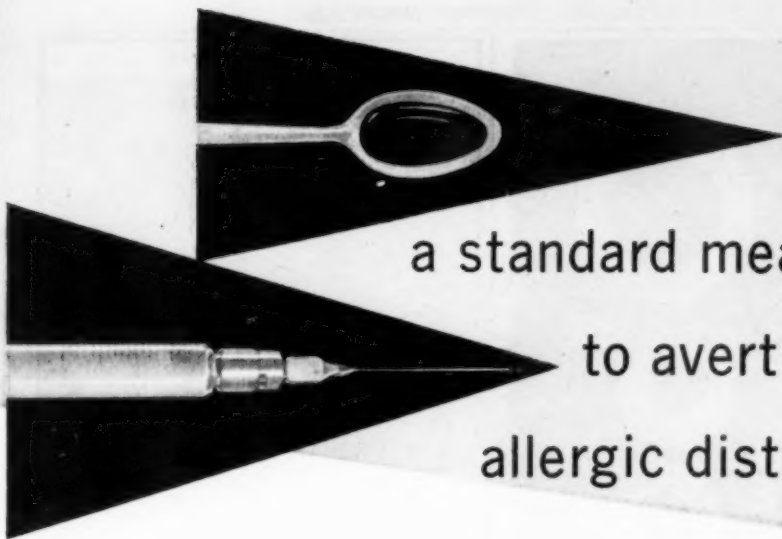
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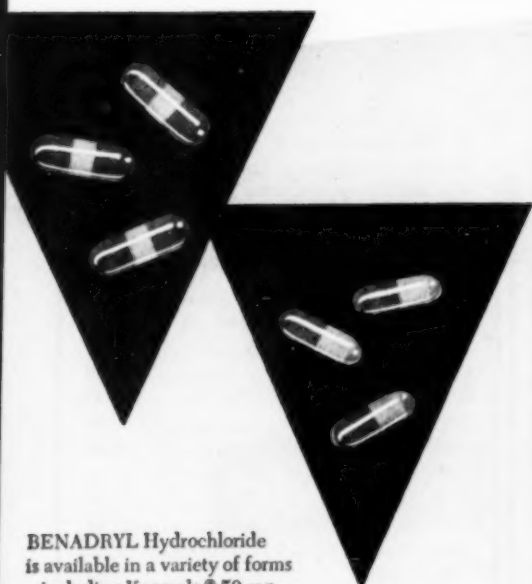
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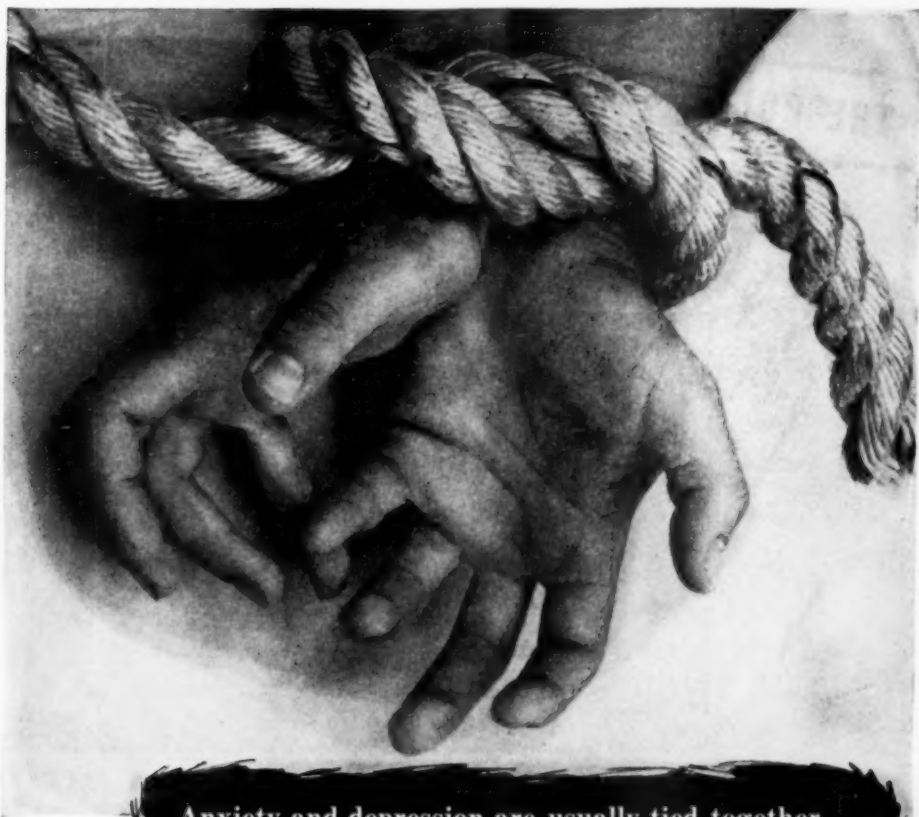
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